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Item 1 of 26
Question Id: 831

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A 23-year-old woman is being evaluated for recurrent episodes of urinary tract infection. She has had 5 episodes of cystitis and an episode of pyelonephritis over the past year. The symptoms tend to occur a few days following sexual intercourse. The patient has no other medical problems and takes no medications. Her temperature is 36.7 C (98 F), blood pressure is 110/70 mm Hg, respirations are 16/min, and pulse is 65/min. Abdominal and genitourinary examinations are normal. Which of the following is the most likely predisposing factor for pyelonephritis in this patient?

A. Frequent voiding
B. Hematogenous bacterial spread
C. Suppression of endogenous flora
D. Urethral colonization
E. Vesicoureteral urine reflux

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A 23-year-old woman is being evaluated for recurrent episodes of urinary tract infection. She has had 5 episodes of cystitis and an episode of pyelonephritis over the past year. The symptoms tend to occur a few days following sexual intercourse. The patient has no other medical problems and takes no medications. Her temperature is 36.7 C (98 F), blood pressure is 110/70 mm Hg, respirations are 16/min, and pulse is 65/min. Abdominal and genitourinary examinations are normal. Which of the following is the most likely predisposing factor for pyelonephritis in this patient?

- A. Frequent voiding (0%)
- B. Hematogenous bacterial spread (1%)
- C. Suppression of endogenous flora (4%)
- D. Urethral colonization (31%)
- ✓ E. Vesicoureteral urine reflux (61%)

Omitted
Correct answer
E

61%
Answered correctly

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Time Spent

01/28/2020
Last Updated

Explanation

The bacteria that usually cause **urinary tract infections (UTIs)** such as cystitis (bladder infection) and pyelonephritis (kidney infection) typically originate from fecal flora and include gram-negative rods (eg, *Escherichia coli, Klebsiella, Proteus*) and *Enterococcus*. In women, sexual intercourse facilitates bacterial ascent up the relatively **short urethra** and into the bladder, which has several antibacterial defenses, including:

- The bladder mucosa normally does not allow bacterial attachment

The bacteria that usually cause **urinary tract infections (UTIs)** such as cystitis (bladder infection) and pyelonephritis (kidney infection) typically originate from fecal flora and include gram-negative rods (eg, *Escherichia coli, Klebsiella, Proteus*) and *Enterococcus*. In women, sexual intercourse facilitates bacterial ascent up the relatively **short urethra** and into the bladder, which has several antibacterial defenses, including:

- The bladder mucosa normally does not allow bacterial attachment
- Normal urine is bactericidal due to high urea content and osmolarity
- **Urine flow** washes the bacteria downstream

When these mechanisms are disrupted or overcome due to bacterial **virulence factors** (eg, fimbriae to facilitate attachment, capsule to resist phagocytosis), **cystitis** occurs.

The normal vesicoureteral junction does not allow retrograde flow of urine. If there is an anatomic abnormality of this area or an increase in bladder pressure, some urine returns to the ureter, carrying any pathogens present in the bladder (**vesicoureteral reflux**). Frequent bladder infections, such as in this patient, may weaken the vesicoureteral junction and facilitate reflux. Without vesicoureteral reflux, the ascent of pathogens to the kidneys is very unlikely, and **pyelonephritis** does not occur.

(Choice A) Frequent voiding may be a symptom of UTI but does not cause the infection. In fact, frequent urination may prevent UTIs by washing pathogens away. Frequency of sexual intercourse is an important risk factor for recurrent UTIs.

(Choice B) Hematogenous bacterial spread is a possible cause of acute pyelonephritis. This mechanism is most significant in hospitalized, elderly, debilitated patients with multiple potential infectious sources or significantly weakened immune defenses. This patient is young and generally healthy with no signs of systemic infection or immunosuppression, making hematogenous spread very unlikely.

(Choices C and D) Normal urethral flora microorganisms (lactobacilli, nonpathogenic staphylococci and streptococci) do not multiply readily in urine and generally do not cause infection. Suppression of this endogenous flora can occur in pregnancy, with antibiotic use, or during a systemic illness and may facilitate distal urethral colonization by pathogenic gram-negative rods. This may play an important role in the development of lower UTIs but generally is not sufficient to cause pyelonephritis.

Educational objective:
Suppression of endogenous flora, colonization of the distal urethra by pathogenic gram-negative rods, and attachment of these pathogens to the bladder mucosa are the stages of pathogenesis in lower urinary tract infections. Anatomic or functional vesicoureteral reflux is almost always

When these mechanisms are disrupted or overcome due to bacterial **virulence factors** (eg, fimbriae to facilitate attachment, capsule to resist phagocytosis), **cystitis** occurs.

The normal vesicoureteral junction does not allow retrograde flow of urine. If there is an anatomic abnormality of this area or an increase in bladder pressure, some urine returns to the ureter, carrying any pathogens present in the bladder (**vesicoureteral reflux**). Frequent bladder infections, such as in this patient, may weaken the vesicoureteral junction and facilitate reflux. Without vesicoureteral reflux, the ascent of pathogens to the kidneys is very unlikely, and **pyelonephritis** does not occur.

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Educational objective:
Suppression of endogenous flora, colonization of the distal urethra by pathogenic gram-negative rods, and attachment of these pathogens to the bladder mucosa are the stages of pathogenesis in lower urinary tract infections. Anatomic or functional vesicoureteral reflux is almost always necessary for the development of acute pyelonephritis.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Urinary tract infection
Subject	System	Topic

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A 72-year-old woman is evaluated due to a month of fatigue and shortness of breath on exertion. The patient has also had lower back pain but no fever or cough. She takes valsartan for hypertension. Temperature is 37.2 C (99 F), blood pressure is 130/80 mm Hg, pulse is 84/min, and respirations are 14/min. On physical examination, the conjunctivae are pale. The remainder of the examination is normal. Laboratory results are as follows:

Hemoglobin	8.2 g/dL
Creatinine	2.1 mg/dL
Calcium	11.2 mg/dL
Total protein	8.5 g/dL
Albumin	3.7 g/dL

X-rays of the lower back demonstrate multiple areas of radiolucency in the L4 and L5 vertebrae. Serum protein electrophoresis reveals a monoclonal gamma globulin spike. Further studies are most likely to show which of the following?

	Parathyroid hormone (PTH)	Urinary calcium	1,25-dihydroxyvitamin D	PTH-related protein
A.	Decreased	Decreased	Normal	Normal
B.	Decreased	Increased	Increased	Normal
C.	Decreased	Increased	Normal	Increased
D.	Decreased	Increased	Decreased	Normal
E.	Increased	Increased	Increased	Normal
F.	Increased	Decreased	Normal	Normal

Hemoglobin	8.2 g/dL
Creatinine	2.1 mg/dL
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A.	Decreased	Decreased	Normal	Normal
B.	Decreased	Increased	Increased	Normal
C.	Decreased	Increased	Normal	Increased
D.	Decreased	Increased	Decreased	Normal
E.	Increased	Increased	Increased	Normal
F.	Increased	Decreased	Normal	Normal

Submit

Hemoglobin	8.2 g/dL
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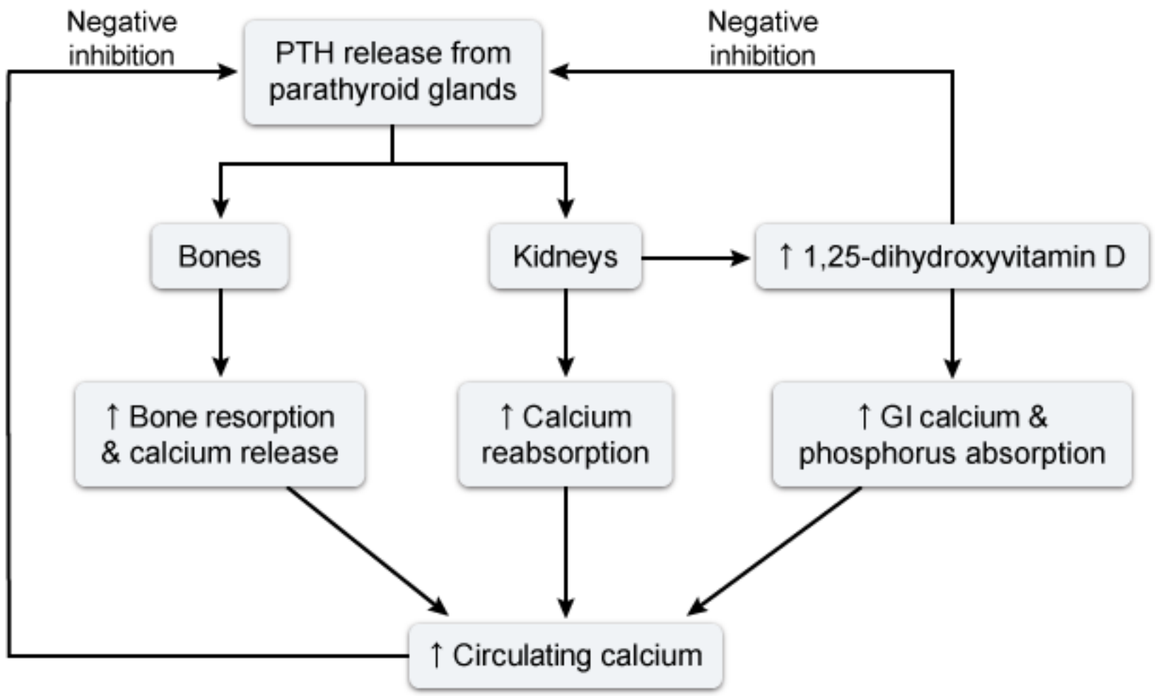
X-rays of the lower back demonstrate multiple areas of radiolucency in the L4 and L5 vertebrae. Serum protein electrophoresis reveals a monoclonal gamma globulin spike. Further studies are most likely to show which of the following?

	Parathyroid hormone (PTH)	Urinary calcium	1,25-dihydroxyvitamin D	PTH-related protein
A. (5%)	Decreased	Decreased	Normal	Normal
B. (9%)	Decreased	Increased	Increased	Normal
C. (18%)	Decreased	Increased	Normal	Increased
✓ D. (51%)	Decreased	Increased	Decreased	Normal
E. (7%)	Increased	Increased	Increased	Normal
F. (7%)	Increased	Decreased	Normal	Normal

PTH, vitamin D & calcium axis



GI = gastrointestinal; **PTH** = parathyroid hormone.

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Multiple myeloma (MM) is a plasma cell malignancy that generates monoclonal immunoglobulin. It is classically characterized by anemia, bone pain/radiolucent lesions, and **hypercalcemia** due to tumor infiltration of the bone marrow; renal insufficiency can also occur due to hypercalcemia and clogging of the renal tubules with immunoglobulin light chains.

MM tumor cells secrete potent **osteolytic cytokines** (eg, tumor necrosis factor-alpha) that liberate calcium from bone and result in hypercalcemia. Elevated serum calcium inhibits the release of parathyroid hormone (PTH) from parathyroid cells, which has several downstream effects including:

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MM tumor cells secrete potent **osteolytic cytokines** (eg, tumor necrosis factor-alpha) that liberate calcium from bone and result in hypercalcemia. Elevated serum calcium inhibits the release of parathyroid hormone (PTH) from parathyroid cells, which has several downstream effects including:

- **Hypercalciuria** – low PTH levels increase urinary calcium excretion due to reduced calcium reabsorption in the distal tubules and collecting ducts of the kidney (where PTH exerts its effects)
- **Low 1,25 dihydroxyvitamin D levels** – low PTH (and renal insufficiency) reduce the activity of renal 1-alpha-hydroxylase, the enzyme that converts 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D (the more active form)

Therefore, patients with MM classically have low PTH and 1,25-dihydroxyvitamin D levels and elevated urinary calcium.

(Choice A) Thiazide diuretics cause hypercalcemia by promoting calcium reabsorption in the distal convoluted tubule. This leads to reduced urinary calcium excretion and low serum PTH levels (elevated serum calcium reduces PTH release). Angiotensin receptor blockers (eg, valsartan) do not increase renal calcium reabsorption.

(Choice B) Granulomatous diseases (eg, sarcoidosis, tuberculosis) can cause hypercalcemia due to production of 1,25-dihydroxyvitamin D by 1-alpha-hydroxylase in granulomatous tissue. This increases the intestinal absorption and urinary excretion of calcium (the latter effect being caused by concomitant suppression of PTH).

(Choice C) Production of PTH-related protein (PTHrP) is the most common cause of hypercalcemia in malignancy (eg, squamous cell carcinoma). PTHrP increases osteoclast activity and renal calcium absorption with minimal effect on 1,25-dihydroxyvitamin D. The hypercalcemia seen in MM is not typically due to PTHrP; it is caused by osteolytic cytokines.

(Choice E) Primary hyperparathyroidism is characterized by excessive PTH release, leading to increased bone resorption and 1,25-dihydroxyvitamin D formation. Urinary calcium excretion is elevated due to the increased filtered calcium load (despite the increased renal reabsorption induced by PTH).

Therefore, patients with MM classically have low PTH and 1,25-dihydroxyvitamin D levels and elevated urinary calcium.

(Choice A) Thiazide diuretics cause hypercalcemia by promoting calcium reabsorption in the distal convoluted tubule. This leads to reduced urinary calcium excretion and low serum PTH levels (elevated serum calcium reduces PTH release). Angiotensin receptor blockers (eg, valsartan) do not increase renal calcium reabsorption.

(Choice B) Granulomatous diseases (eg, sarcoidosis, tuberculosis) can cause hypercalcemia due to production of 1,25-dihydroxyvitamin D by 1-alpha-hydroxylase in granulomatous tissue. This increases the intestinal absorption and urinary excretion of calcium (the latter effect being caused by concomitant suppression of PTH).

(Choice C) Production of PTH-related protein (PTHrP) is the most common cause of hypercalcemia in malignancy (eg, squamous cell carcinoma). PTHrP increases osteoclast activity and renal calcium absorption with minimal effect on 1,25-dihydroxyvitamin D. The hypercalcemia seen in MM is not typically due to PTHrP; it is caused by osteolytic cytokines.

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(Choice F) Familial hypocalciuric hypercalcemia is caused by inactivating mutations of the Ca^{2+}-sensing receptor in the nephron and parathyroid glands. Renal calcium reabsorption is increased (urinary calcium excretion is low) and higher serum calcium levels are required to suppress PTH release (serum PTH is slightly elevated or inappropriately normal).

Educational objective:
Multiple myeloma is associated with increased bone resorption due to the production of tumor-related cytokines. This results in elevated serum calcium levels, which reduce parathyroid hormone (PTH) production. Low PTH decreases renal calcium reabsorption (hypercalciuria), and, in combination with renal insufficiency, reduces 1,25-dihydroxyvitamin D synthesis.

References

- Multiple myeloma: from diagnosis to treatment.

Pathophysiology Renal, Urinary Systems & Electrolytes Hypercalcemia

A 34-year-old woman comes to the hospital with a 4-day history of abdominal cramps, nausea, and watery diarrhea. Today she developed dizziness on standing. Her child has had similar symptoms recently. The patient has no prior medical conditions and takes no medications on a regular basis. Blood pressure is 124/82 mm Hg while supine and 100/70 on standing; pulse is 98/min. Examination shows dry mucous membranes. The abdomen is soft and nontender. Laboratory results are as follows:

Serum chemistry	
Sodium	144 mEq/L
Blood urea nitrogen	50 mg/dL
Creatinine	1.8 mg/dL
Urinalysis	
Protein	negative
Red blood cells	0/hpf
White blood cells	0-1/hpf
Microscopy	few hyaline casts
Urine sodium	8 mEq/L

Which of the following changes are most likely to be seen in this patient?

	Vasopressin	Norepinephrine	Angiotensin II	Endothelin 1
A.	↑	↑	↑	↑

Urinalysis

Protein	negative
Red blood cells	0/hpf
White blood cells	0-1/hpf
Microscopy	few hyaline casts

Urine sodium	8 mEq/L

Which of the following changes are most likely to be seen in this patient?

	Vasopressin	Norepinephrine	Angiotensin II	Endothelin 1
A.	↑	↑	↑	↑
B.	↑	↑	↑	↓
C.	↓	↑	↑	↓
D.	↑	↓	↓	↑
E.	↓	↓	↓	↓
F.	↑	↓	↑	↓

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Urinalysis

Protein	negative
Red blood cells	0/hpf
White blood cells	0-1/hpf
Microscopy	few hyaline casts
Urine sodium	8 mEq/L

Which of the following changes are most likely to be seen in this patient?

	Vasopressin	Norepinephrine	Angiotensin II	Endothelin 1
✓ A. (51%)	↑	↑	↑	↑
B. (27%)	↑	↑	↑	↓
C. (6%)	↓	↑	↑	↓
D. (5%)	↑	↓	↓	↑
E. (4%)	↓	↓	↓	↓
F. (5%)	↑	↓	↑	↓

Explanation

This patient with gastroenteritis has evidence of **hypovolemia** (dry mucous membranes, orthostatic dizziness/hypotension) and acute kidney injury. Decreased extracellular fluid volume stimulates compensatory mechanisms directed at maintaining systemic blood pressure and tissue oxygenation. This is largely driven by the sympathetic nervous system and the kidneys:

- Activation of the **renin-angiotensin-aldosterone system** (RAAS) leads to elevated levels of **angiotensin II** (ATII), a potent vasoconstrictor that stimulates the release of aldosterone and **endothelin 1**. These increase sodium and water reabsorption and systemic vascular resistance to help maintain blood pressure.
- **Vasopressin** (antidiuretic hormone) is released by the posterior pituitary in response to increased serum osmolarity and decreased systemic pressure; it increases urea and free water reabsorption by the renal collecting duct.
- **Increased sympathetic activity** results in release of circulating **norepinephrine** and other catecholamines, which increases systemic vasoconstriction, renal sodium and water reabsorption, and heart rate.

These neurohumoral mechanisms promote volume expansion and increase blood pressure, helping to maintain tissue perfusion. Laboratory studies characteristically reflect sodium, water, and urea reabsorption by the kidney, including **low urine sodium** (<20 mEq/L), low fractional excretion of sodium (<1%), and **elevated blood urea nitrogen to creatinine ratio** (>20:1). Urinary sediment is typically bland or may show hyaline casts (which suggest increased urine concentration).

Educational objective:
Hypovolemia triggers a variety of compensatory mechanisms to improve tissue perfusion. These include activation of the renin-angiotensin-aldosterone system (resulting in increased aldosterone and endothelin release), increased vasopressin release, and increased sympathetic tone.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Prerenal azotemia
Subject	System	Topic

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Item 4 of 26
Question Id: 1050

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A 34-year-old male who is being treated for acute leukemia develops oliguria. His serum creatinine level is 2.7 mg/dL. Renal biopsy reveals multiple uric acid crystals obstructing renal tubular lumen. The principal site of uric acid precipitation would be which of the following?

A. Proximal tubules due to high solute concentration

B. Proximal tubules due to impaired uric acid transport

C. Loop of Henle due to urine hyposmolarity

D. Distal tubules due to high urine flow rate

E. Collecting ducts due to low urine pH

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A 34-year-old male who is being treated for acute leukemia develops oliguria. His serum creatinine level is 2.7 mg/dL. Renal biopsy reveals multiple uric acid crystals obstructing renal tubular lumen. The principal site of uric acid precipitation would be which of the following?

A. Proximal tubules due to high solute concentration (25%)

B. Proximal tubules due to impaired uric acid transport (19%)

C. Loop of Henle due to urine hyposmolarity (6%)

D. Distal tubules due to high urine flow rate (3%)

✓ E. Collecting ducts due to low urine pH (44%)

Omitted
Correct answer
E

44%
Answered correctly

03 secs
Time Spent

02/03/2020
Last Updated

Explanation

Tumor lysis syndrome is an oncologic emergency. It often develops during chemotherapy for high-grade lymphomas, leukemias, and other tumors that have rapid cell turnover and high sensitivity to chemotherapy. When a large number of tumor cells are destroyed during chemotherapy, intracellular ions, such as potassium, phosphorous, and uric acid (a metabolite of tumor nucleic acid), are released into the serum and are then filtered by the kidneys.

Uric acid (pKa = 5.4) is soluble at physiologic pH, but precipitates in an acidic environment. The lowest pH along the nephron is found in the distal tubules and collecting ducts; so these are the segments of the nephron that become obstructed by uric acid crystals. Obstructive uropathy and acute renal failure follow.

Tumor lysis syndrome is an oncologic emergency. It often develops during chemotherapy for high-grade lymphomas, leukemias, and other tumors that have rapid cell turnover and high sensitivity to chemotherapy. When a large number of tumor cells are destroyed during chemotherapy, intracellular ions, such as potassium, phosphorous, and uric acid (a metabolite of tumor nucleic acid), are released into the serum and are then filtered by the kidneys.

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The risk of tumor lysis syndrome can be reduced by urine alkalinization and hydration. Additionally, allopurinol (a xanthine oxidase inhibitor) is used to reduce uric acid production during the breakdown of tumor cells.

(Choice D) Ignore the anatomy portion of choice D and evaluate the latter portion. A "high urine flow rate" would universally decrease uric acid crystallization and precipitation. Therefore, this cannot possibly be the correct answer.

(Choices A, B and C) Uric acid does not precipitate in proximal tubules or in Henle's loop.

Educational Objective:
Tumor lysis syndrome occurs when tumors with a high cell turnover are treated with chemotherapy. The lysis of tumor cells causes intracellular ions, such as potassium and phosphorous, and uric acid (metabolite of tumor nucleic acid) to be released into serum. Uric acid is soluble at physiologic pH, but it can precipitate in the normally acidic environment of distal tubules and collecting ducts. The prevention of tumor lysis syndrome includes urine alkalinization and hydration, as high urine flow and high pH along the nephron prevents crystallization and precipitation of uric acid.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Tumor lysis syndrome
Subject	System	Topic

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A 32-year-old man comes to the emergency department due to sudden onset of severe right flank pain that radiates toward the groin. He also has gross hematuria but no fever or dysuria. The patient has no significant medical conditions and has never experienced similar symptoms. He takes no medications. Temperature is 36.7 C (98.1 F), blood pressure is 120/80 mm Hg, and pulse is 88/min. The right flank is tender to palpation. There is no costovertebral angle tenderness. Imaging shows a stone in the middle of the right ureter. Which of the following is most likely to be seen on laboratory evaluation of this patient?

- A. Hypercalcemia, hypercalciuria
- B. Hyperuricemia, hyperuricosuria
- C. Normocalcemia, hypercalciuria
- D. Normocalcemia, hyperoxaluria
- E. Normouricemia, hyperuricosuria

Submit

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- A. Hypercalcemia, hypercalciuria (13%)
- B. Hyperuricemia, hyperuricosuria (2%)
- ✓ C. Normocalcemia, hypercalciuria (62%)
- D. Normocalcemia, hyperoxaluria (19%)
- E. Normouricemia, hyperuricosuria (2%)

Omitted
Correct answer
C

62%
Answered correctly

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Explanation

Calcium stones represent 75%-80% of all renal calculi and include calcium oxalate and calcium phosphate stones. **Hypercalciuria** is the most common risk factor for calcium stones in adults.

In most patients, the hypercalciuria is **idiopathic**. Factors can include increased gastrointestinal absorption, increased mobilization of calcium from bone, or decreased renal tubular calcium reabsorption. However, in the absence of an underlying metabolic disorder (eg,

Explanation

Calcium stones represent 75%-80% of all renal calculi and include calcium oxalate and calcium phosphate stones. **Hypercalciuria** is the most common risk factor for calcium stones in adults.

In most patients, the hypercalciuria is **idiopathic**. Factors can include increased gastrointestinal absorption, increased mobilization of calcium from bone, or decreased renal tubular calcium reabsorption. However, in the absence of an underlying metabolic disorder (eg, hyperparathyroidism), most patients remain **normocalcemic** due to regulation of plasma calcium levels by vitamin D and parathyroid hormone.

(Choice A) Hypercalcemia with resulting hypercalciuria may occur in primary hyperparathyroidism, sarcoidosis, malignancy, and chronic acidemia. However, these are less common causes of nephrolithiasis, and this patient has no symptoms of hypercalcemia (eg, fatigue, constipation) or clinical features to suggest a disorder that might cause hypercalcemia.

(Choices B and E) Hyperuricosuria with hyperuricemia can occur with myeloproliferative disorders, tumor lysis syndrome, gout, and Lesch-Nyhan syndrome. High-protein diets typically cause hyperuricosuria with normouricemia. Hyperuricosuria can cause uric acid stone formation and also predisposes to calcium nephrolithiasis (uric acid precipitation acts as a nidus for calcium deposition).

(Choice D) Hyperoxaluria can result from a diet high in oxalate (found in foods such as chocolate, nuts, and spinach). Low-calcium diets and intestinal malabsorption syndromes such as Crohn disease can also cause hyperoxaluria as both cause less calcium to be available to bind and trap oxalate in the gut. Hyperoxaluria is a less common risk factor for calcium stone formation than hypercalciuria.

Educational objective:
Hypercalciuria is the most common risk factor for calcium (calcium oxalate and calcium phosphate) kidney stones in adults; contributing factors may include increased gastrointestinal absorption, increased mobilization of calcium from bone, or decreased renal tubular calcium reabsorption. However, most patients remain normocalcemic due to regulation of plasma calcium levels by vitamin D and parathyroid hormone.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Renal calculi
Subject	System	Topic

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Item 6 of 26
Question Id: 1577

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A 21-year-old male presents to his physician after noticing that his urine had a "frothy" appearance. He also complains of easy fatigability and anorexia. His past medical history is significant only for an upper respiratory infection several weeks ago. Physical examination reveals symmetric pitting edema of the ankles. Which of the following is most likely decreased in this patient?

A. Capillary hydrostatic pressure

B. Interstitial fluid pressure

C. Plasma oncotic pressure

D. Tissue lymphatic drainage

E. Circulating aldosterone level

Submit

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A 21-year-old male presents to his physician after noticing that his urine had a "frothy" appearance. He also complains of easy fatigability and anorexia. His past medical history is significant only for an upper respiratory infection several weeks ago. Physical examination reveals symmetric pitting edema of the ankles. Which of the following is most likely decreased in this patient?

A. Capillary hydrostatic pressure (5%)

B. Interstitial fluid pressure (3%)

✓ C. Plasma oncotic pressure (83%)

D. Tissue lymphatic drainage (5%)

E. Circulating aldosterone level (1%)

Omitted
Correct answer
C

83%
Answered correctly

02 secs
Time Spent

02/03/2020
Last Updated

Explanation

Frothy, foamy urine may be caused by proteinuria or bile salts in the urine. This patient's history of a recent upper respiratory infection and ankle edema on physical exam suggest a diagnosis of nephrotic syndrome with associated low serum albumin. Hypoalbuminemia lowers the plasma oncotic pressure and causes interstitial edema formation due to net plasma filtration. Minimal change disease (MCD) is the most common cause of nephrosis in children, and can occur in adults as well.

(Choice A) A decrease in capillary hydrostatic pressure would tend to decrease net plasma filtration and interstitial edema formation.

Explanation

Frothy, foamy urine may be caused by proteinuria or bile salts in the urine. This patient's history of a recent upper respiratory infection and ankle edema on physical exam suggest a diagnosis of nephrotic syndrome with associated low serum albumin. Hypoalbuminemia lowers the plasma oncotic pressure and causes interstitial edema formation due to net plasma filtration. Minimal change disease (MCD) is the most common cause of nephrosis in children, and can occur in adults as well.

(Choice A) A decrease in capillary hydrostatic pressure would tend to decrease net plasma filtration and interstitial edema formation.

(Choice B) This patient's ankle edema is the result of a transudate of plasma into the interstitial tissues of the ankle. We would therefore expect an increase in the steady state interstitial fluid pressure in the ankles.

(Choice D) While a primary decrease in lymphatic drainage can cause interstitial edema, the rate of lymphatic drainage would be increased in this particular patient because of the accumulation of ankle interstitial fluid.

(Choice E) In nephrotic syndrome, the plasma oncotic pressure is decreased, which causes net plasma filtration into the interstitium, thus decreasing the effective circulating intravascular volume. This reduction of the intravascular volume stimulates a compensatory increase in the activity of the renin-angiotensin-aldosterone system. Patients with nephrotic syndrome tend to have elevated circulating aldosterone levels.

Educational Objective:
Frothy or foamy urine may be caused by proteinuria. Heavy proteinuria, as in nephrotic syndrome, can cause regional or generalized interstitial edema because the decrease in serum albumin and total protein concentrations lowers the plasma oncotic pressure and increases net plasma filtration in capillary beds.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Glomerular disorders
Subject	System	Topic

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A 36-year-old woman comes to the office due to frequent urination since an exacerbation of multiple sclerosis 2 months ago. Most of her symptoms, including dizziness, leg weakness, and numbness, have improved with corticosteroid treatment. However, she has continued difficulty holding urine, and on several occasions has passed a small amount of urine while trying to reach the bathroom. She has no urine leakage during coughing or sneezing. The patient has no other medical problems. Her abdomen is soft and nontender. Neurological examination shows hyperreflexia and increased tone in the lower extremities. Her postvoid residual volume is low.

Glucose, serum	160 mg/dL
Urinalysis	
Blood	negative
Leukocyte esterase	negative
Bacteria	none
White blood cells	3-4/HPF

Which of the following is the most likely explanation for her urinary symptoms?

A. Detrusor muscle weakness

B. Hyperglycemia-induced osmotic diuresis

C. Low-grade cystitis causing bladder irritation

D. Pelvic floor laxity and urethral sphincter dysfunction

E. Uninhibited bladder contraction

symptoms, including dizziness, leg weakness, and numbness, have improved with corticosteroid treatment. However, she has continued difficulty holding urine, and on several occasions has passed a small amount of urine while trying to reach the bathroom. She has no urine leakage during coughing or sneezing. The patient has no other medical problems. Her abdomen is soft and nontender. Neurological examination shows hyperreflexia and increased tone in the lower extremities. Her postvoid residual volume is low.

Glucose, serum	160 mg/dL
Urinalysis	
Blood	negative
Leukocyte esterase	negative
Bacteria	none
White blood cells	3-4/HPF

Which of the following is the most likely explanation for her urinary symptoms?

- A. Detrusor muscle weakness (11%)
- B. Hyperglycemia-induced osmotic diuresis (8%)
- C. Low-grade cystitis causing bladder irritation (4%)
- D. Pelvic floor laxity and urethral sphincter dysfunction (13%)
- ✓ E. Uninhibited bladder contraction (62%)

Omitted
Correct answer

62%
Answered correctly

03 secs
Time Spent

03/16/2020
Last Updated

Explanation

Differential diagnosis of urinary incontinence		
	Etiology	**Symptoms**
Stress	↓ Urethral sphincter tone Urethral hypermobility	Leakage with coughing, lifting, sneezing
Urge	Detrusor hyperactivity	Sudden, overwhelming urge to urinate
Overflow	Impaired detrusor contractility Bladder outlet obstruction	Incomplete emptying & persistent involuntary dribbling

This patient's presentation is consistent with **urge incontinence**, which is due to detrusor overactivity causing a sudden and/or frequent urge to urinate and empty the bladder. The micturition reflex is an autonomic spinal reflex mediated by both sensory and motor fibers from nerve centers at the S2-S4 levels. Parasympathetic stimulation causes detrusor muscle contraction and internal urethral sphincter relaxation. Sympathetic fibers cause internal sphincter contraction and also help with sensing a full bladder.

Multiple sclerosis (MS) is likely an autoimmune disease that causes varying degrees of demyelination, inflammation, and gliosis in the central nervous system (eg, optic nerves, spinal cord, brainstem, periventricular white matter, and cerebellum). Regions in the pons and cerebral cortex partially inhibit the micturition reflex and also regulate contraction/relaxation of the external urethral sphincter. Spinal cord lesions above the sacral region cause a loss of higher center control of micturition and lead to detrusor hyperreflexia and urge incontinence. Patients typically develop a frequent urge to urinate and pass a small amount of urine. As the disease progresses, the bladder can become atonic and dilated leading to overflow incontinence.

(Choice A) Overflow incontinence can be due to impaired detrusor contractility or bladder outlet obstruction (eg, tumor obstructing urethra). Patients usually develop involuntary and continuous urinary leakage when the bladder is full and often have incomplete emptying. Post-void residual urine volume is usually high.

(Choice B) Osmotic diuresis due to hyperglycemia can occur in uncontrolled diabetes mellitus and causes polyuria. However, it more commonly

	Bladder outlet obstruction	

This patient's presentation is consistent with **urge incontinence**, which is due to detrusor overactivity causing a sudden and/or frequent urge to urinate and empty the bladder. The micturition reflex is an autonomic spinal reflex mediated by both sensory and motor fibers from nerve centers at the S2-S4 levels. Parasympathetic stimulation causes detrusor muscle contraction and internal urethral sphincter relaxation. Sympathetic fibers cause internal sphincter contraction and also help with sensing a full bladder.

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(Choice A) Overflow incontinence can be due to impaired detrusor contractility or bladder outlet obstruction (eg, tumor obstructing urethra). Patients usually develop involuntary and continuous urinary leakage when the bladder is full and often have incomplete emptying. Post-void residual urine volume is usually high.

(Choice B) Osmotic diuresis due to hyperglycemia can occur in uncontrolled diabetes mellitus and causes polyuria. However, it more commonly occurs with blood sugar >250 mg/dL. This patient's blood sugar of 160 mg/dL and absence of glycosuria make this less likely.

(Choice C) Bladder infection (cystitis) can cause irritation of the bladder wall and findings similar to urge incontinence with urinary urgency, frequency, and incontinence. However, this patient's relatively normal urinalysis (no leukocyte esterase, hematuria, or bacteria seen) makes this less likely. Up to 5 wbc/hpf is normal.

(Choice D) Stress incontinence occurs in patients with sphincter dysfunction or weakness when intraabdominal pressure exceeds the urethral sphincter pressure (eg, sneezing, coughing), causing involuntary urine leakage. This patient's absence of urinary leakage with coughing or sneezing makes this less likely.

Educational objective:
Patients with multiple sclerosis most commonly develop urge incontinence due to loss of central nervous system inhibition of detrusor contraction

frequent urge to urinate and pass a small amount of urine. As the disease progresses, the bladder can become atonic and dilated leading to overflow incontinence.

(Choice A) Overflow incontinence can be due to impaired detrusor contractility or bladder outlet obstruction (eg, tumor obstructing urethra). Patients usually develop involuntary and continuous urinary leakage when the bladder is full and often have incomplete emptying. Post-void residual urine volume is usually high.

(Choice B) Osmotic diuresis due to hyperglycemia can occur in uncontrolled diabetes mellitus and causes polyuria. However, it more commonly occurs with blood sugar >250 mg/dL. This patient's blood sugar of 160 mg/dL and absence of glycosuria make this less likely.

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Educational objective:
Patients with multiple sclerosis most commonly develop urge incontinence due to loss of central nervous system inhibition of detrusor contraction in the bladder. As the disease progresses, the bladder can become atonic and dilated, leading to overflow incontinence.

References

- Multiple sclerosis produces significant changes in urinary bladder innervation which are partially reflected in the lower urinary tract functional status-sensory nerve fibers role in detrusor overactivity.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Urinary incontinence
Subject	System	Topic

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Scientists studying the kidney's response to hypoperfusion apply a clip to a pig's right renal artery that reduces blood flow to the kidney by about 70%. After 6 months, they perform a right nephrectomy and examine the glomeruli and tubules microscopically. Which of the following cell types would be most likely to undergo hyperplasia as a result of the clip placement?

A. Cuboidal epithelial cells of the proximal tubules

B. Endothelial cells of the efferent arteriole

C. Intraglomerular mesangial cells

D. Modified smooth muscle cells of the afferent arteriole

E. Squamous epithelial cells of the thick ascending limb of the loop of Henle

Submit

Scientists studying the kidney's response to hypoperfusion apply a clip to a pig's right renal artery that reduces blood flow to the kidney by about 70%. After 6 months, they perform a right nephrectomy and examine the glomeruli and tubules microscopically. Which of the following cell types would be most likely to undergo hyperplasia as a result of the clip placement?

A. Cuboidal epithelial cells of the proximal tubules (10%)

B. Endothelial cells of the efferent arteriole (22%)

C. Intraglomerular mesangial cells (20%)

✓ D. Modified smooth muscle cells of the afferent arteriole (43%)

E. Squamous epithelial cells of the thick ascending limb of the loop of Henle (2%)

Omitted
Correct answer
D

43%
Answered correctly

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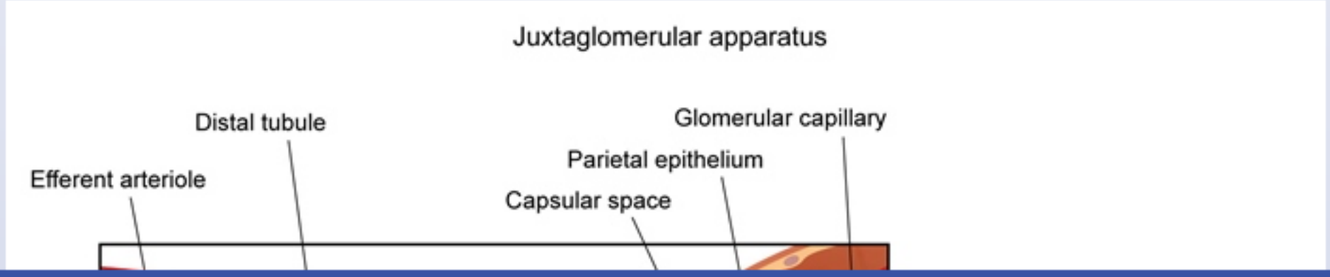
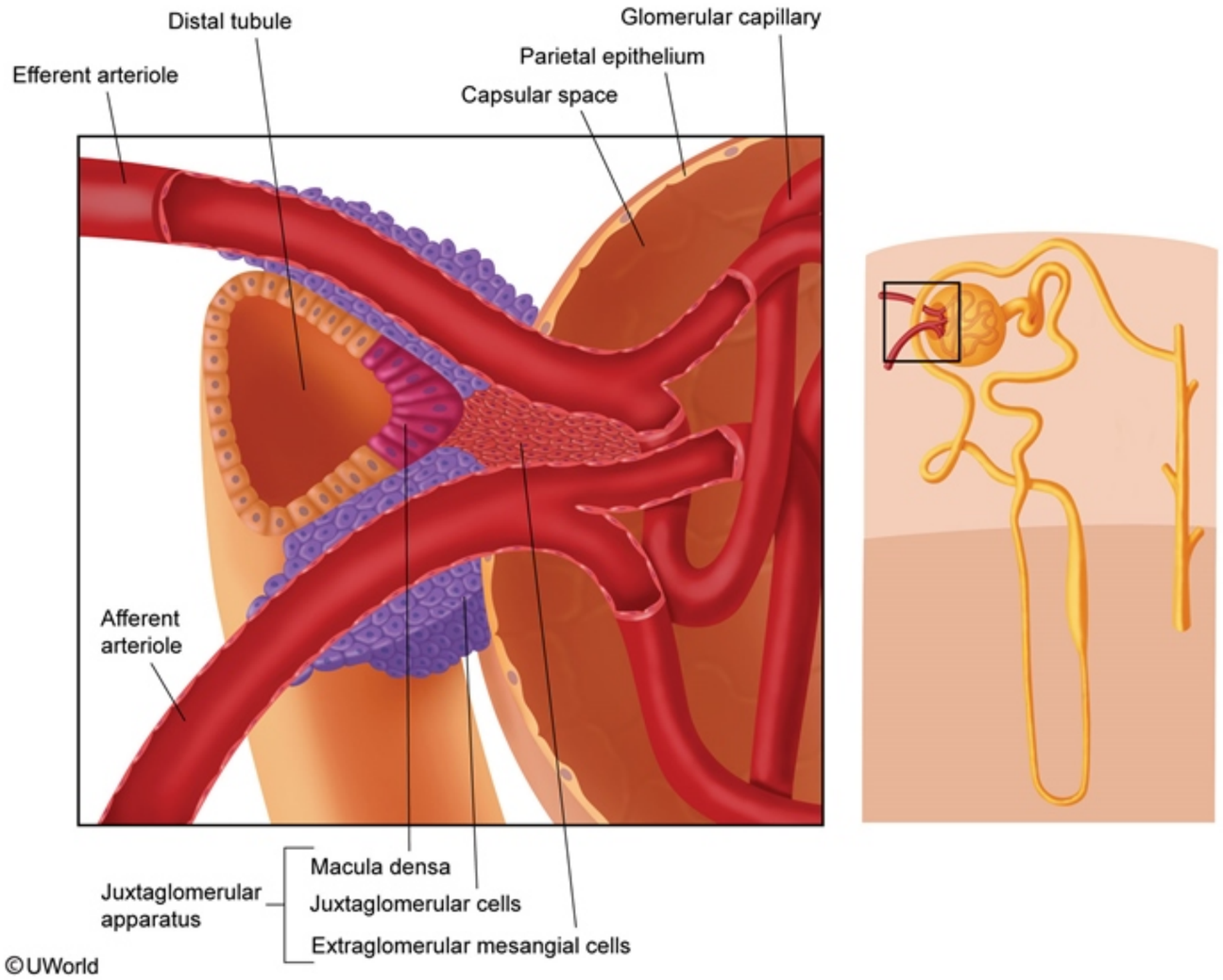
Time Spent

04/28/2020
Last Updated

Explanation



Juxtaglomerular apparatus



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A markedly narrowed renal artery (eg, due to an atherosclerotic plaque or external clip) cannot supply the kidney with enough blood to maintain a normal glomerular filtration rate. The reduced blood flow is sensed by the juxtaglomerular (JG) apparatus, which consists of the macula densa, extraglomerular mesangial cells (ie, Lacis cells), and JG cells. **Macula densa** cells are tall, narrow cells located in the **distal tubule** that monitor salt content and tubular flow rate. This information is transmitted to nearby **JG cells** that are located mainly in the wall of the **afferent arteriole**. JG cells are **modified smooth muscle cells** with renin-containing zymogen granules.

Significant **renal hypoperfusion** leads to a compensatory **increase in renin secretion** by JG cells. This activates the renin-angiotensin-aldosterone system, leading to increased levels of angiotensin II and aldosterone. Long-term renal hypoperfusion, such as caused by renal artery stenosis, leads the JG cells of the affected kidney(s) to undergo **hyperplasia** as a result of chronic stimulation.

When renal artery stenosis is restricted to one side and the contralateral kidney functions normally, chronic kidney disease does not occur as the normal kidney is still able to efficiently filter and excrete waste products (eg, creatinine, urea). However, hypertension can occur in both unilateral and bilateral disease, as secretion of renin by one kidney will lead to systemic vasoconstriction and retention of salt and water by both kidneys.

(Choices A, C, and E) The cuboidal cells of the proximal tubule, the intraglomerular mesangial cells (which are distinct from the extraglomerular mesangial [Lacis] cells), and the squamous cells of the thick ascending limb of the loop of Henle are not components of the JG apparatus and do not undergo hyperplasia in response to hypoperfusion. In fact, these tissues may atrophy in the clipped kidney due to ischemia.

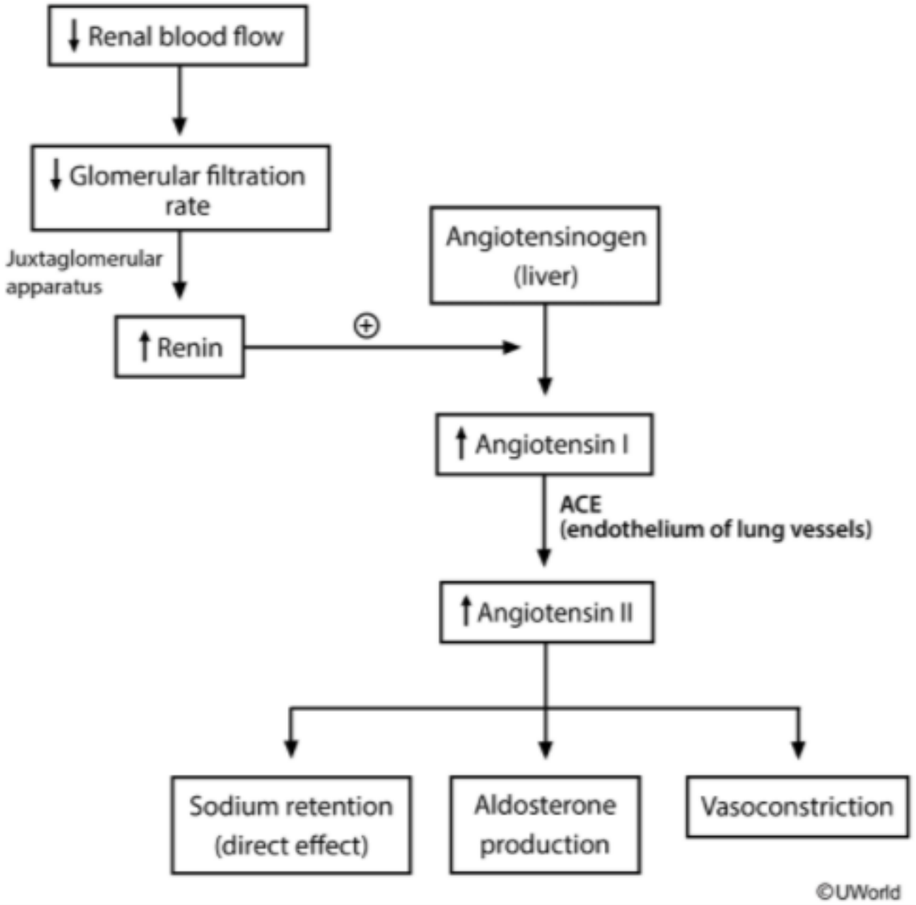
(Choice B) The endothelium is composed of a single layer of squamous cells that line blood vessel walls; endothelial cells do not undergo hyperplasia in response to hypoperfusion. Efferent arteriolar smooth muscle cells may undergo hypertrophy/hyperplasia with chronic angiotensin stimulation, but these lie within the arteriolar wall (underneath the endothelium).

Educational objective:
Renal artery stenosis causing significant renal hypoperfusion will result in a decreased glomerular filtration rate and activation of the renin-angiotensin-aldosterone system. This leads to increased renin release by modified smooth muscle (juxtaglomerular) cells in the walls of afferent glomerular arterioles. Chronic renal hypoperfusion can cause hyperplasia of the juxtaglomerular apparatus.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Renal artery stenosis
Subject	System	Topic

Exhibit Display

Renin-angiotensin system



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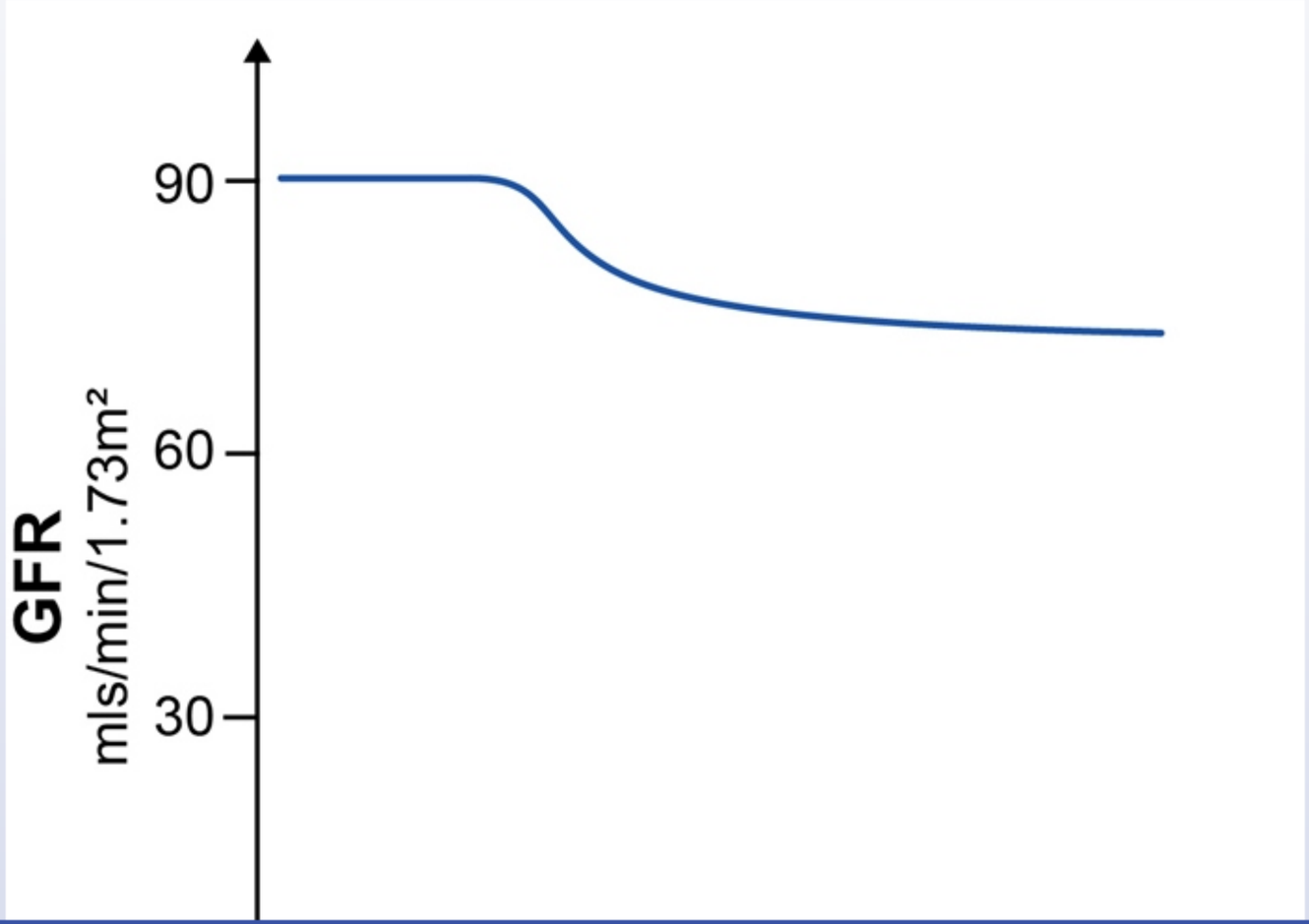
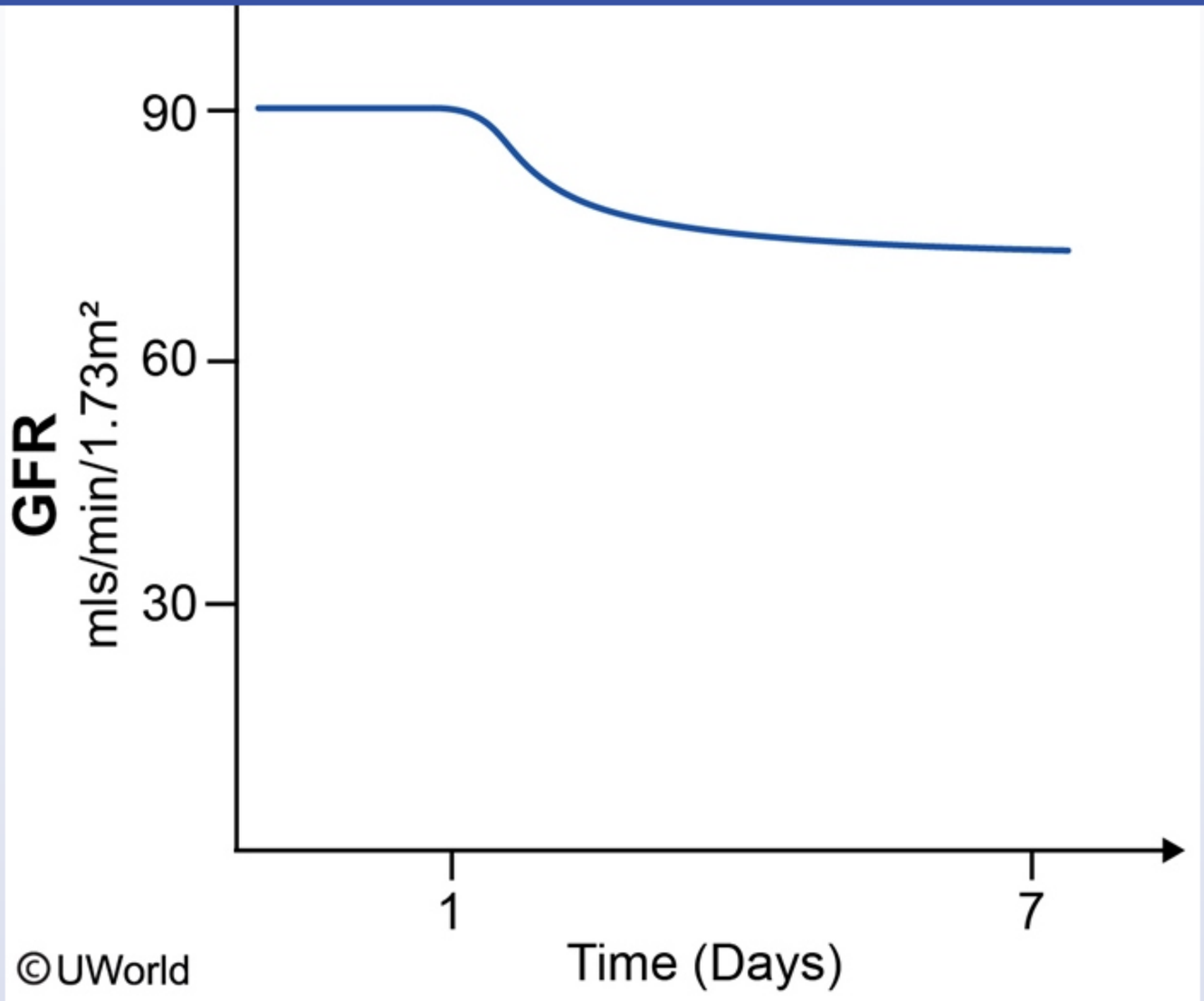
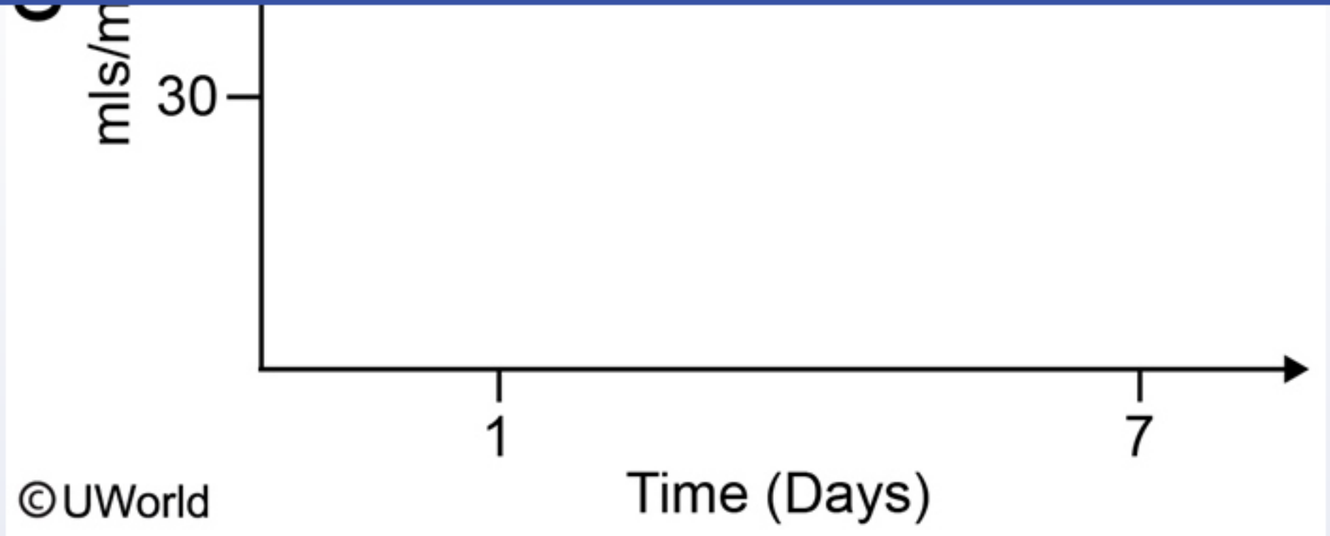
Subject System Topic

A 44-year-old man comes to the office for a routine check-up. Past medical history is significant for hypercholesterolemia, which he has controlled through diet. His father died of a myocardial infarction at age 56, and his mother, who is still living, has a history of stroke. On physical examination, the patient's blood pressure is 160/100 mm Hg and heart rate is 70/min. He is started on enalapril. During the first 7 days of therapy, the patient's glomerular filtration rate (GFR) adjusts as shown in the graph below.





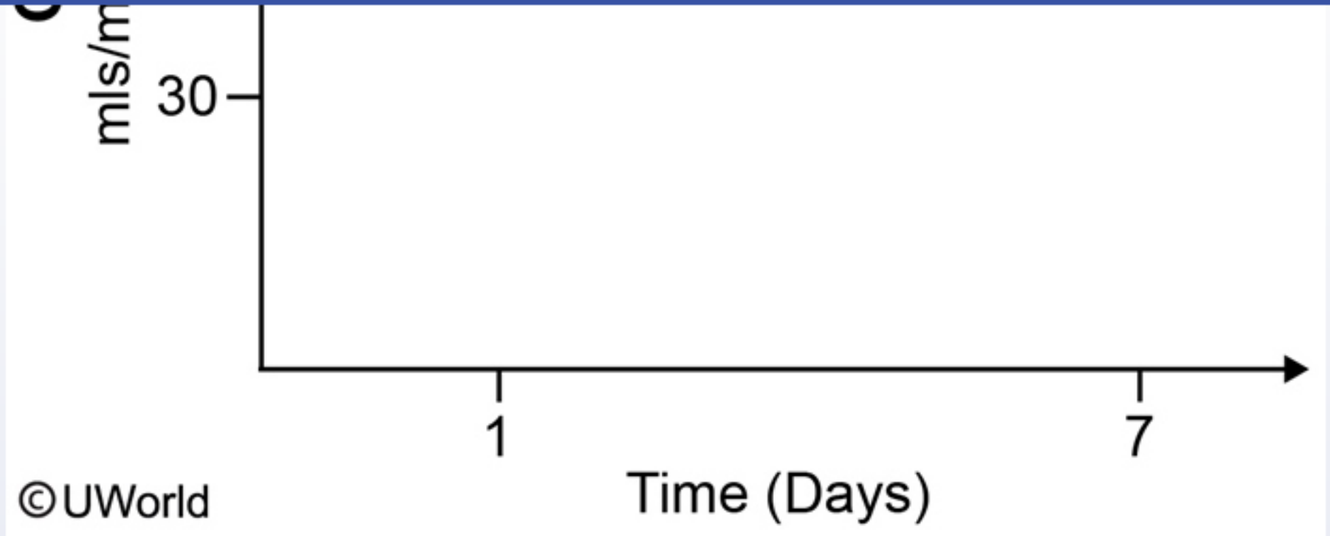
Which of the following structures was most likely affected by a downstream effect of enalapril and is therefore responsible for this patient's renal



Which of the following structures was most likely affected by a downstream effect of enalapril and is therefore responsible for this patient's renal response?

- A. Afferent arterioles
- B. Distal tubules
- C. Efferent arterioles
- D. Proximal tubules
- E. Vasa recta

Submit



Which of the following structures was most likely affected by a downstream effect of enalapril and is therefore responsible for this patient's renal response?

- A. Afferent arterioles (12%)
- B. Distal tubules (2%)
- ✓ C. Efferent arterioles (83%)
- D. Proximal tubules (1%)
- E. Vasa recta (0%)

Omitted
Correct answer

83%
Answered correctly

06 secs
Time Spent

06/29/2020
Last Updated

Omitted
Correct answer
C

83%
Answered correctly

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Last Updated

Explanation

Enalapril is an angiotensin-converting-enzyme **(ACE) inhibitor**. All ACE inhibitors decrease circulating levels of angiotensin II, a substance that causes the following:

- Systemic vasoconstriction
- Preferential constriction of the glomerular efferent arteriole
- Enhancement of adrenal aldosterone secretion

As a result, **reduced angiotensin II** production in patients taking an ACE inhibitor would be expected to acutely **decrease efferent arteriolar resistance** and systemic vascular resistance. Selective efferent arteriolar dilation combined with the decreased renal perfusion pressure causes a **reduction in glomerular filtration rate**.

Educational objective:
In the kidney, angiotensin II preferentially constricts the efferent arteriole, thereby maintaining the glomerular filtration rate (GFR) within normal range. ACE-inhibitors promote efferent arteriolar dilation, causing GFR reduction.

Pathophysiology	Renal, Urinary Systems & Electrolytes	ACE inhibitors
Subject	System	Topic

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A 62-year-old woman with long-standing type 2 diabetes mellitus experiences progressive renal decline over 4-5 years despite optimal blood pressure control. She is started on interim hemodialysis and eventually undergoes transplantation of a deceased donor renal allograft. Three weeks following surgery, she experiences generalized malaise. Her past medical history is significant for diabetic retinopathy and osteoporosis, and her current medications include mycophenolate and tacrolimus. Laboratory results are as follows:

Potassium	5.2 mEq/L
Blood urea nitrogen	45 mg/dL
Creatinine	3.1 mg/dL
Glucose	123 mg/dL
Calcium	10.0 mg/dL

She undergoes percutaneous biopsy of the transplanted kidney; light microscopy findings are shown below.

Which of the following is the most likely cause of this patient's current condition?

A. Cell-mediated immunity

B. Drug toxicity

C. Immune complex vasculitis

D. Renovascular disease

E. Volume depletion

Submit

weeks following surgery, she experiences generalized malaise. Her past medical history is significant for diabetic retinopathy and osteoporosis, and her current medications include mycophenolate and tacrolimus. Laboratory results are as follows:

Potassium	5.2 mEq/L
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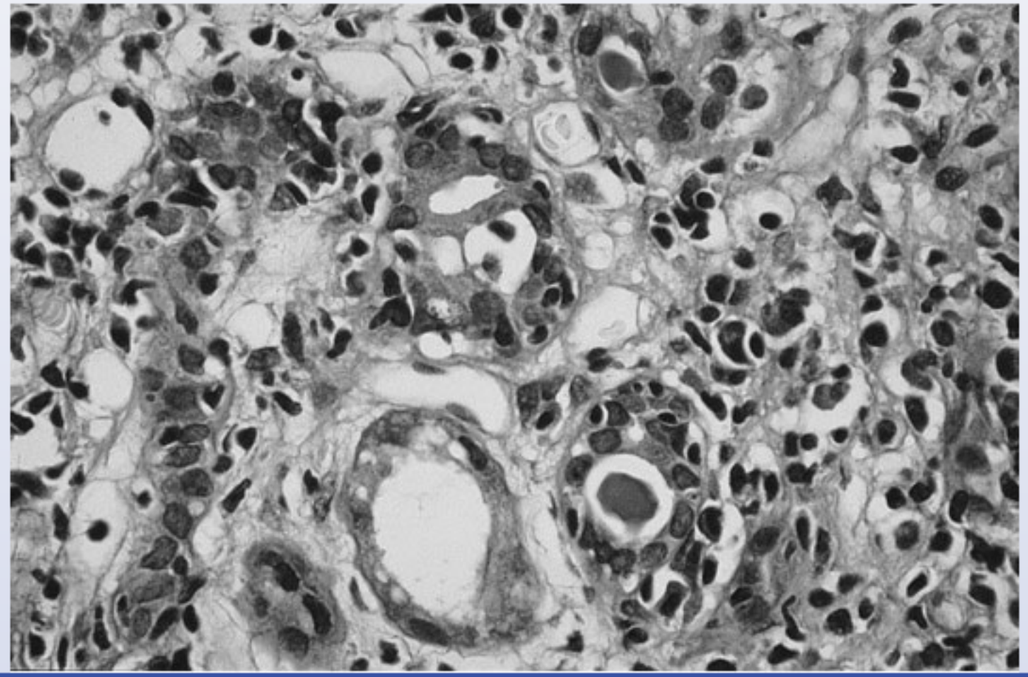
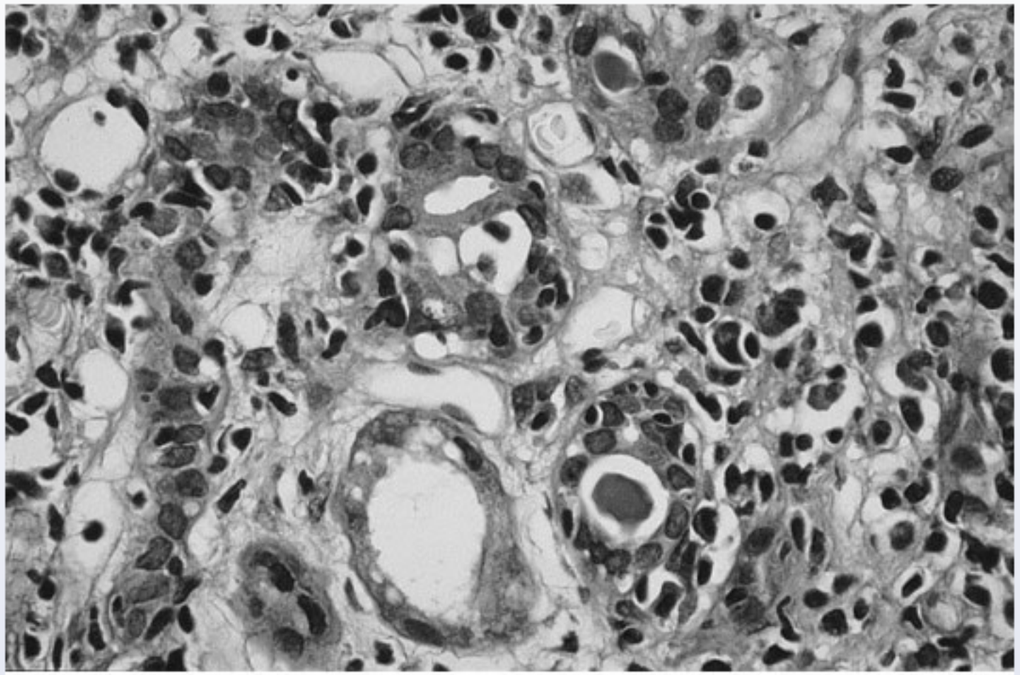


She undergoes percutaneous biopsy of the transplanted kidney; light microscopy findings are shown below.



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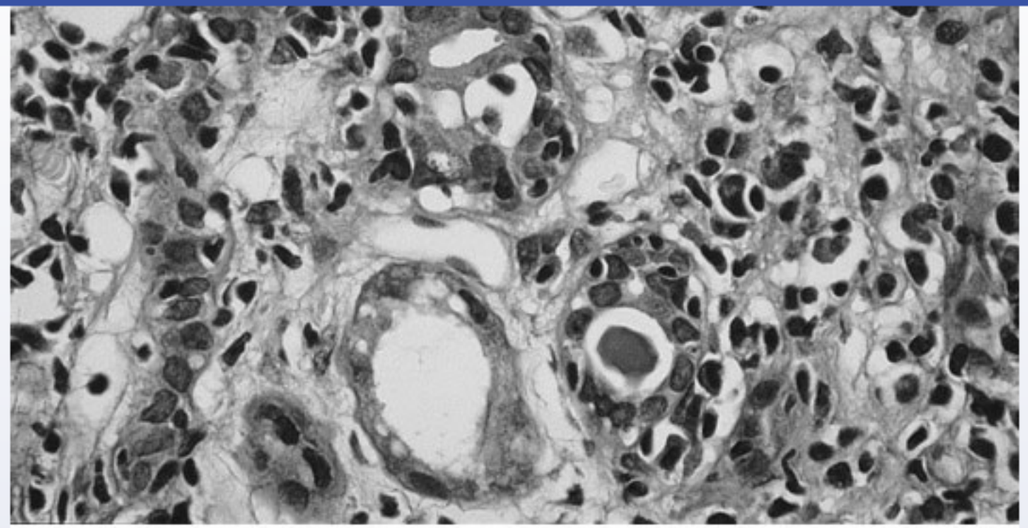
Which of the following is the most likely cause of this patient's current condition?

- A. Cell-mediated immunity
- B. Drug toxicity
- C. Immune complex vasculitis
- D. Renovascular disease
- E. Volume depletion



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Which of the following is the most likely cause of this patient's current condition?

- ✓ A. Cell-mediated immunity (62%)
- B. Drug toxicity (16%)
- C. Immune complex vasculitis (13%)
- D. Renovascular disease (6%)
- E. Volume depletion (1%)

Omitted
Correct answer

62%
Answered correctly

07 secs
Time Spent

04/11/2020
Last Updated

Explanation

Transplant rejection reactions			
Type of rejection	**Onset time**	**Etiology**	**Morphology**
Hyperacute	Minutes to hours	• Preformed recipient antibodies against graft antigens	• Gross mottling & cyanosis • Arterial fibrinoid necrosis & capillary thrombotic occlusion
Acute	Usually <6 months	• Exposure to donor antigens induces activation of naive immune cells • Predominantly **cell-mediated**	• **Cellular:** lymphocytic interstitial infiltrate & endotheliitis • Humoral: C4d deposition, neutrophilic infiltrate, necrotizing vasculitis
Chronic	Months to years	• Chronic low-grade immune response refractory to immunosuppression • Predominantly **humoral**	• Vascular wall thickening & luminal narrowing • Interstitial fibrosis & parenchymal atrophy

Acute rejection is usually seen within the first 6 months after renal transplant, with most episodes occurring in the early postoperative period. Patients experiencing acute rejection are typically asymptomatic, but some develop fever, chills, malaise, and arthralgias. Other manifestations of acute rejection include **increased serum creatinine**, hypertension, and reduced urine output. Acute rejection can be antibody- or cell-mediated. The latter is associated with a **lymphocytic infiltrate** of the vessels (endotheliitis), tubules, and renal interstitium (diffusely increased cellularity). Mycophenolate and tacrolimus are immunosuppressant drugs commonly prescribed in early posttransplantation patients to reduce the risk of acute rejection.

(Choice B) Calcineurin inhibitors (eg, cyclosporine, tacrolimus) can reduce renal blood flow and cause direct damage to renal endothelial and tubular cells. Histologic findings typically include early arteriolar hyalinization and tubular vacuolization. Despite their nephrotoxicity, these agents remain beneficial for preventing acute kidney rejection.

		• Predominantly **humoral**	

Acute rejection is usually seen within the first 6 months after renal transplant, with most episodes occurring in the early postoperative period. Patients experiencing acute rejection are typically asymptomatic, but some develop fever, chills, malaise, and arthralgias. Other manifestations of acute rejection include **increased serum creatinine**, hypertension, and reduced urine output. Acute rejection can be antibody- or cell-mediated. The latter is associated with a **lymphocytic infiltrate** of the vessels (endotheliitis), tubules, and renal interstitium (diffusely increased cellularity). Mycophenolate and tacrolimus are immunosuppressant drugs commonly prescribed in early posttransplantation patients to reduce the risk of acute rejection.

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(Choice C) Immune complex vasculitis develops in conditions such as systemic lupus erythematosus and Henoch-Schönlein purpura and can cause a proliferative glomerulonephritis characterized by increased glomerular cellularity.

(Choice D) Patients with chronic renovascular disease (eg, renal artery stenosis) usually develop diffuse ischemic changes, including interstitial fibrosis, crowding of the glomeruli, and tubular atrophy.

(Choice E) Severe volume depletion can cause acute kidney injury characterized by necrosis of the tubular epithelial cells on biopsy. Lymphocytic infiltration would not be seen.

Educational objective:
Acute renal allograft rejection can be an antibody- or cell-mediated process. Acute cellular rejection is associated with diffuse lymphocytic infiltration of the renal vasculature (endotheliitis), tubules, and interstitium.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Kidney transplantation
Subject	System	Topic

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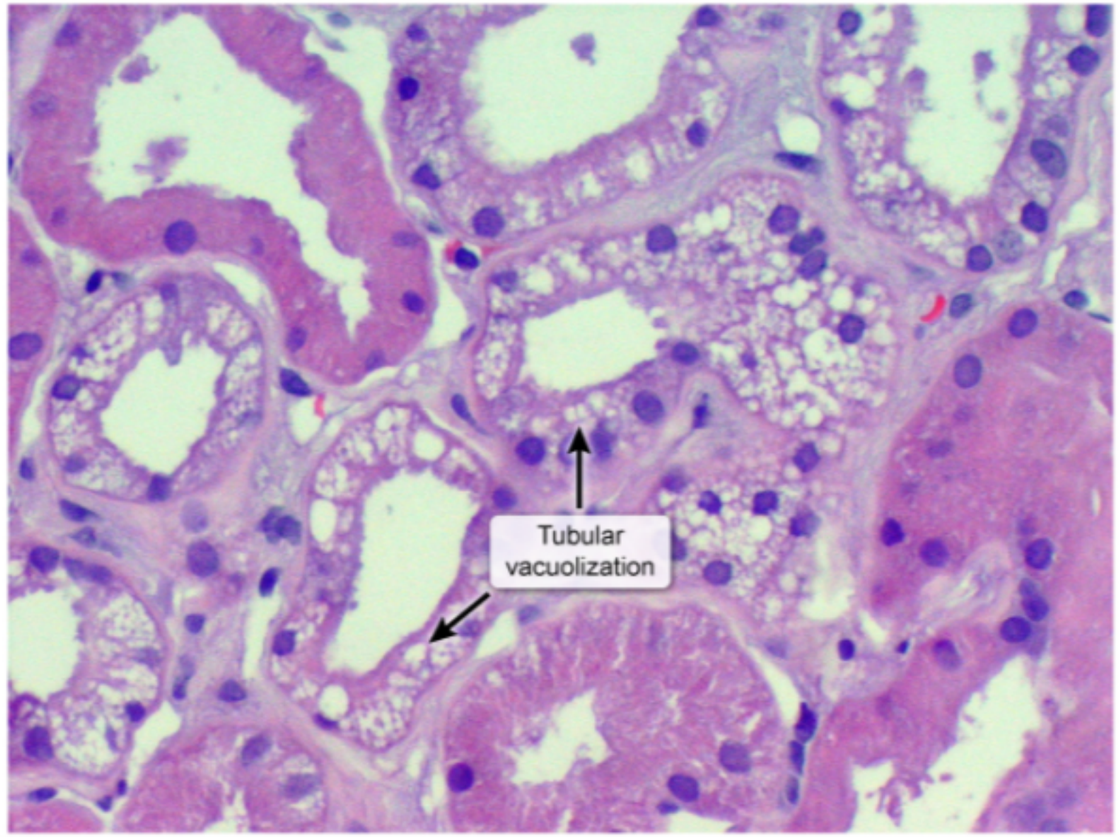
• Predominantly humoral

Exhibit Display

Calcineurin toxicity



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Item 10 of 26
Question Id: 11064

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- Predominantly humoral

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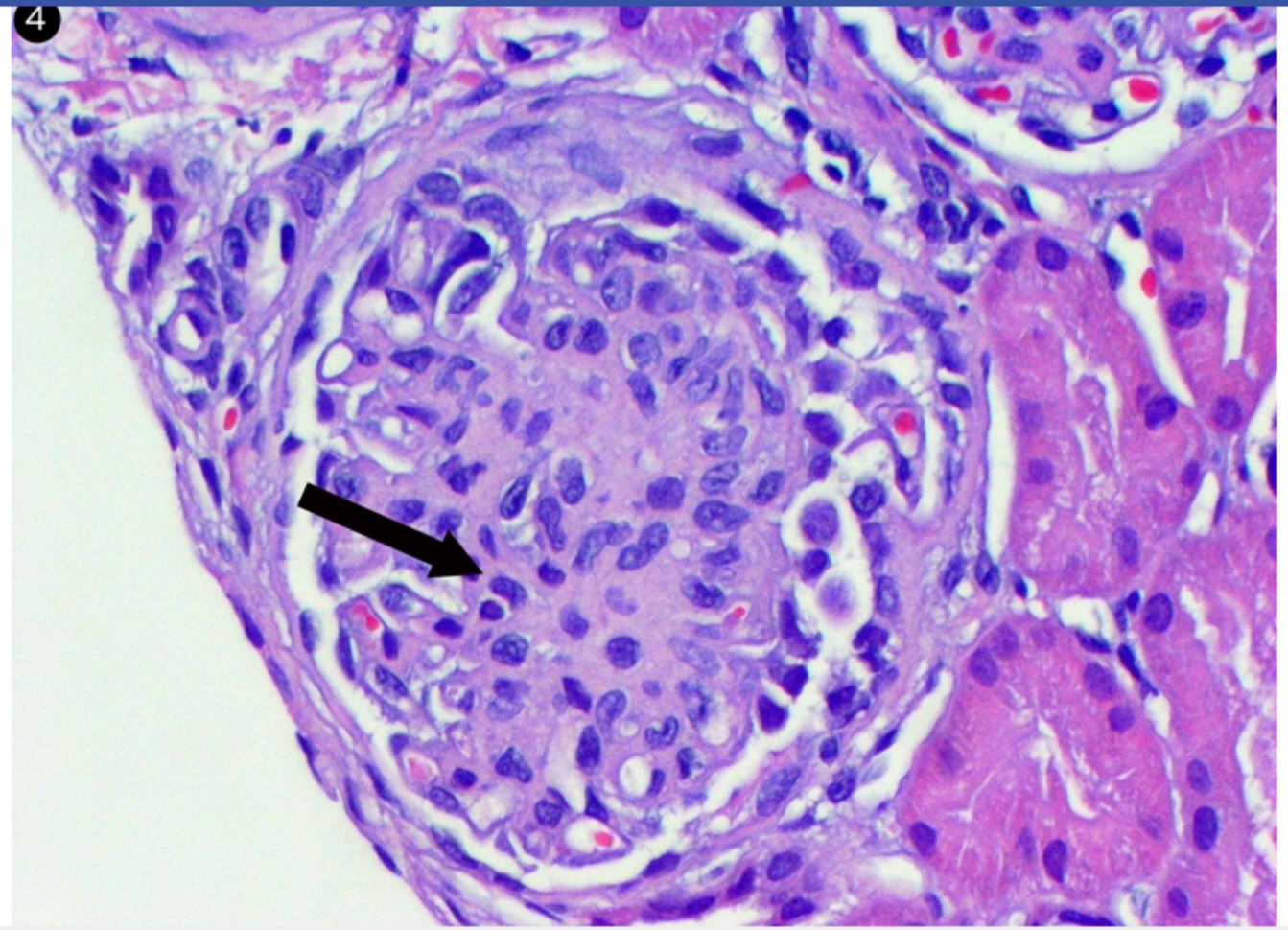

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A 58-year-old man comes to the office due to fatigue, decreased appetite, muscle cramps, and nausea. The patient has chronic kidney disease resulting from primary focal segmental glomerulosclerosis. His current medications include a vitamin D supplement. While his blood pressure is being obtained, the patient develops carpal spasm. Bilateral lower extremity pedal edema is noted. Laboratory evaluation shows a blood urea nitrogen level of 120 mg/dL, serum creatinine level of 10 mg/dL, and serum calcium level of 6 mg/dL. Which of the following is most likely contributing to this patient's carpal spasm?

A. Hyperphosphatemia

B. Hypoparathyroidism

C. Low albumin level

D. Low fibroblast growth factor 23 level

E. Vitamin D toxicity

Submit

A 58-year-old man comes to the office due to fatigue, decreased appetite, muscle cramps, and nausea. The patient has chronic kidney disease resulting from primary focal segmental glomerulosclerosis. His current medications include a vitamin D supplement. While his blood pressure is being obtained, the patient develops carpal spasm. Bilateral lower extremity pedal edema is noted. Laboratory evaluation shows a blood urea nitrogen level of 120 mg/dL, serum creatinine level of 10 mg/dL, and serum calcium level of 6 mg/dL. Which of the following is most likely contributing to this patient's carpal spasm?

- ✓ A. Hyperphosphatemia (64%)
- B. Hypoparathyroidism (21%)
- C. Low albumin level (5%)
- D. Low fibroblast growth factor 23 level (2%)
- E. Vitamin D toxicity (5%)

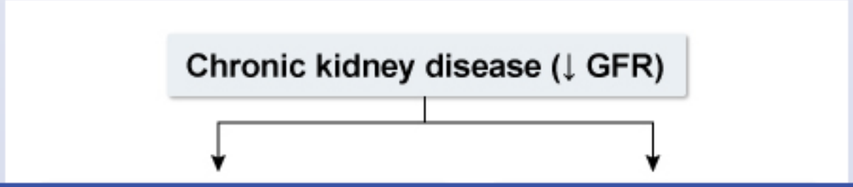
Omitted
Correct answer
A

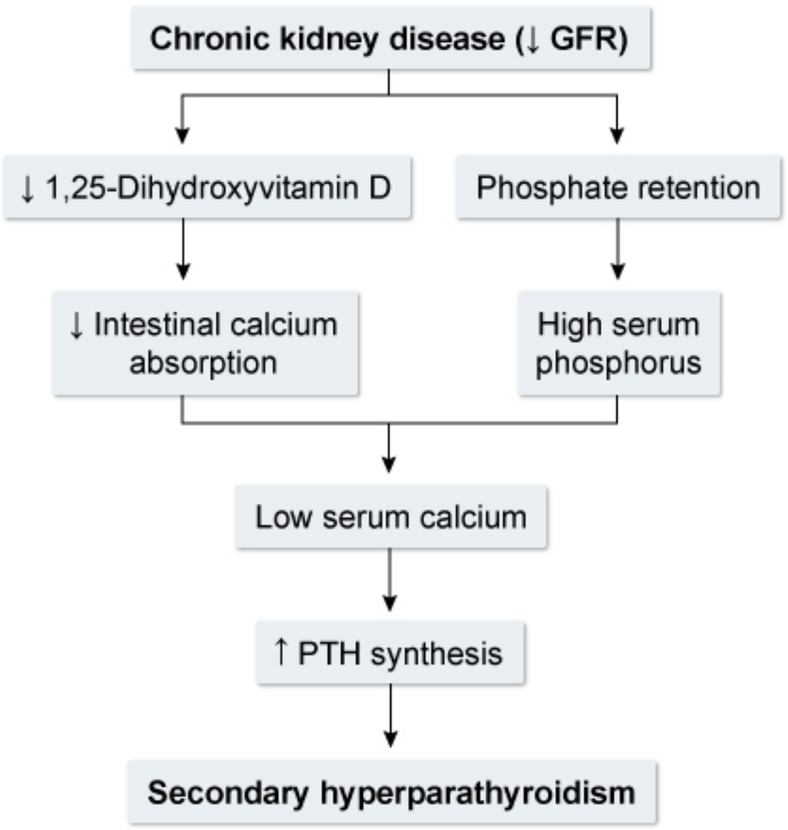
64%
Answered correctly

02 secs
Time Spent

04/07/2020
Last Updated

Explanation





GFR = glomerular filtration rate; **PTH** = parathyroid hormone.

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This patient with **chronic kidney disease** (CKD) has developed carpal spasm secondary to hypocalcemia. In CKD, reduced filtration and excretion of phosphorus causes **hyperphosphatemia**, which induces **hypocalcemia** through the following mechanisms:

- Released phosphate binds to free calcium and precipitates in soft tissues (which, over the long term, can lead to vascular calcification and stiffness)

This patient with **chronic kidney disease** (CKD) has developed carpal spasm secondary to hypocalcemia. In CKD, reduced filtration and excretion of phosphorus causes **hyperphosphatemia**, which induces **hypocalcemia** through the following mechanisms:

- Released phosphate binds to free calcium and precipitates in soft tissues (which, over the long term, can lead to vascular calcification and stiffness)
- Increased serum phosphate triggers the release of fibroblast growth factor 23 from bone, which acts to lower phosphate levels in part by inhibiting renal expression of 1-alpha hydroxylase. This reduces production of 1,25-hydroxyvitamin D (calcitriol), leading to reduced intestinal calcium absorption

Hypocalcemia is also worsened by the progressive loss of functioning renal tissue in CKD, which further reduces calcitriol synthesis.

Hypocalcemia can cause alterations in cellular membrane potentials and **neuromuscular excitability**. Manifestations include muscle cramps, Chvostek (**facial twitching** elicited by tapping on the facial nerve) and Trousseau (**carpal spasm** triggered by inflation of a blood pressure cuff around the arm) signs, hyperreflexia, QTc prolongation, and seizures.

(Choice B) The hypocalcemia and hyperphosphatemia that occur in patients with CKD stimulate secretion of parathyroid hormone (ie, secondary hyperparathyroidism). By contrast, hypoparathyroidism is usually due to autoimmune disease or iatrogenic injury during thyroid surgery and is not a common finding in CKD.

(Choice C) Serum calcium is composed of an ionized free calcium fraction and a protein-bound (largely to albumin) fraction; only ionized calcium is metabolically active. Hypoalbuminemia can occur in patients with nephrotic syndrome (eg, this patient with focal segmental glomerulosclerosis). However, although hypoalbuminemia lowers the bound fraction (and therefore total serum calcium), ionized calcium remains normal, and patients do not experience hypocalcemic symptoms.

(Choice D) Fibroblast growth factor 23 levels are usually low in patients with normal phosphate metabolism but are increased in patients with renal failure in response to hyperphosphatemia.

(Choice E) Vitamin D toxicity can occur in food faddists, patients with mental illness, and those inadvertently treated with excessive doses of vitamin D. However, this causes hypercalcemia, not hypocalcemia.

Educational objective:

Chvostek (**facial twitching** elicited by tapping on the facial nerve) and Trousseau (**carpal spasm** triggered by inflation of a blood pressure cuff around the arm) signs, hyperreflexia, QTc prolongation, and seizures.

(Choice B) The hypocalcemia and hyperphosphatemia that occur in patients with CKD stimulate secretion of parathyroid hormone (ie, secondary hyperparathyroidism). By contrast, hypoparathyroidism is usually due to autoimmune disease or iatrogenic injury during thyroid surgery and is not a common finding in CKD.

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(Choice D) Fibroblast growth factor 23 levels are usually low in patients with normal phosphate metabolism but are increased in patients with renal failure in response to hyperphosphatemia.

(Choice E) Vitamin D toxicity can occur in food faddists, patients with mental illness, and those inadvertently treated with excessive doses of vitamin D. However, this causes hypercalcemia, not hypocalcemia.

Educational objective:
In chronic kidney disease, reduced excretion of phosphate can cause hyperphosphatemia. This induces hypocalcemia directly by binding free calcium and depositing in tissues, and indirectly by triggering fibroblast growth factor 23 secretion (decreases calcitriol production and intestinal calcium absorption). The resulting hypocalcemia can manifest as neuromuscular excitability (eg, carpal spasm).

References

- Pathophysiology of calcium, phosphorus, and magnesium dysregulation in chronic kidney disease.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Chronic kidney disease
Subject	System	Topic

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Item 11 of 26
Question Id: 15289

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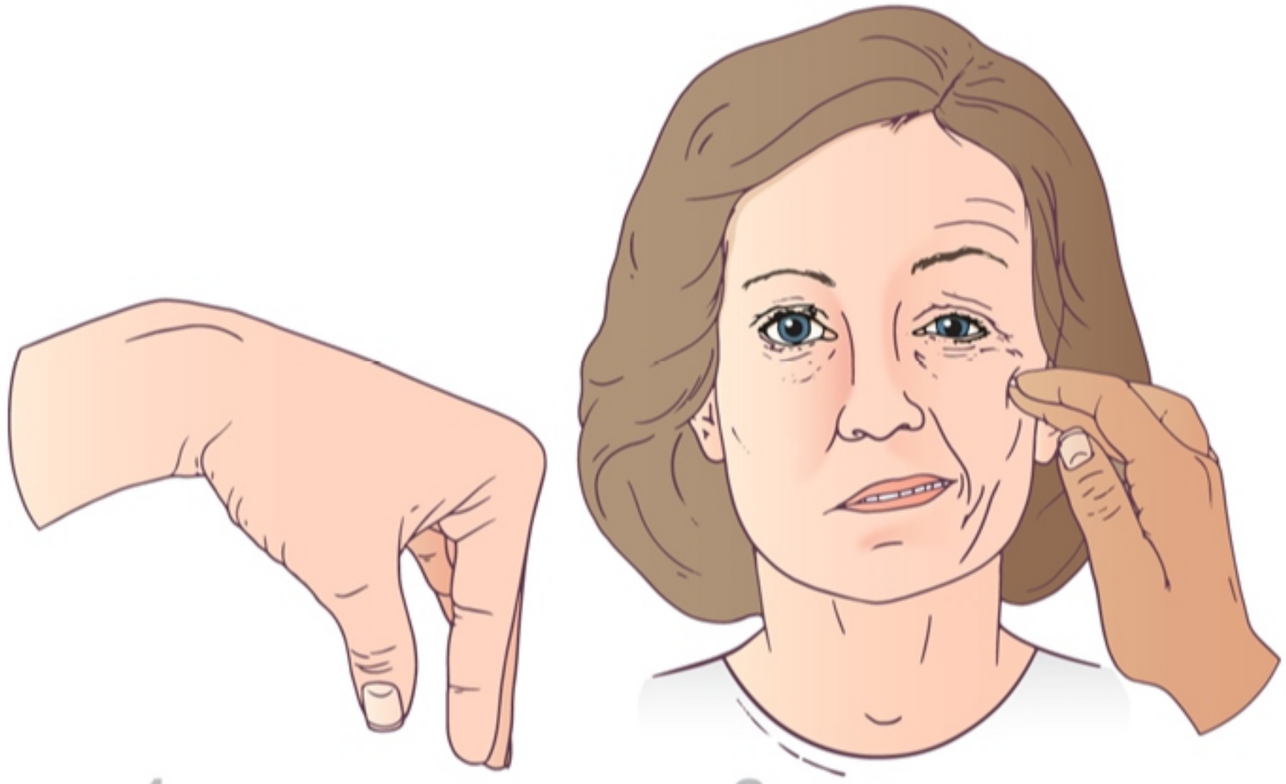
This patient with **chronic kidney disease** (CKD) has developed carpal spasm secondary to hypocalcemia. In CKD, reduced filtration and

Exhibit Display

Signs of hypocalcemia



1 Trousseau sign

2 Chvostek sign

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In chronic kidney disease, reduced excretion of phosphate can cause hyperphosphatemia. This induces hypocalcemia directly by binding free

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A 44-year-old man is brought to the hospital with fatigue, shortness of breath, and lethargy. The patient had a brief upper respiratory illness about a month ago but began experiencing progressive dyspnea on exertion 2 weeks ago. He has no significant medical history and takes no medications. Blood pressure is 100/70 mm Hg; pulse is 95/min and regular. The apical impulse is palpated in the sixth intercostal space along the left anterior axillary line. An S3 is heard on cardiac auscultation. Bibasilar crackles are present. Distal extremities are cold to touch and there is 1+ peripheral edema. Laboratory results are as follows:

Blood urea nitrogen	45 mg/dL
Serum creatinine	1.8 mg/dL
Urine microscopy	
Red blood cells	0/hpf
White blood cells	0-1/hpf
Sediment	none seen

Which of the following is likely to be present in this patient compared to the normal state?

- A. Decreased distal tubule sodium reabsorption
- B. Decreased proximal tubule urea reabsorption
- C. Decreased renal venous pressure
- D. Increased collecting duct free water excretion
- E. Increased proximal tubular sodium reabsorption
- F. Increased renal blood flow

left anterior axillary line. An S3 is heard on cardiac auscultation. Bibasilar crackles are present. Distal extremities are cold to touch and there is 1+ peripheral edema. Laboratory results are as follows:

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D. Increased collecting duct free water excretion
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Submit

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Blood urea nitrogen	45 mg/dL
Serum creatinine	1.8 mg/dL
Urine microscopy	
Red blood cells	0/hpf
White blood cells	0-1/hpf
Sediment	none seen

Which of the following is likely to be present in this patient compared to the normal state?

A. Decreased distal tubule sodium reabsorption (9%)
B. Decreased proximal tubule urea reabsorption (7%)
C. Decreased renal venous pressure (17%)
D. Increased collecting duct free water excretion (6%)
✓ E. Increased proximal tubular sodium reabsorption (55%)
F. Increased renal blood flow (3%)

Omitted
Correct answer

55%
Answered correctly

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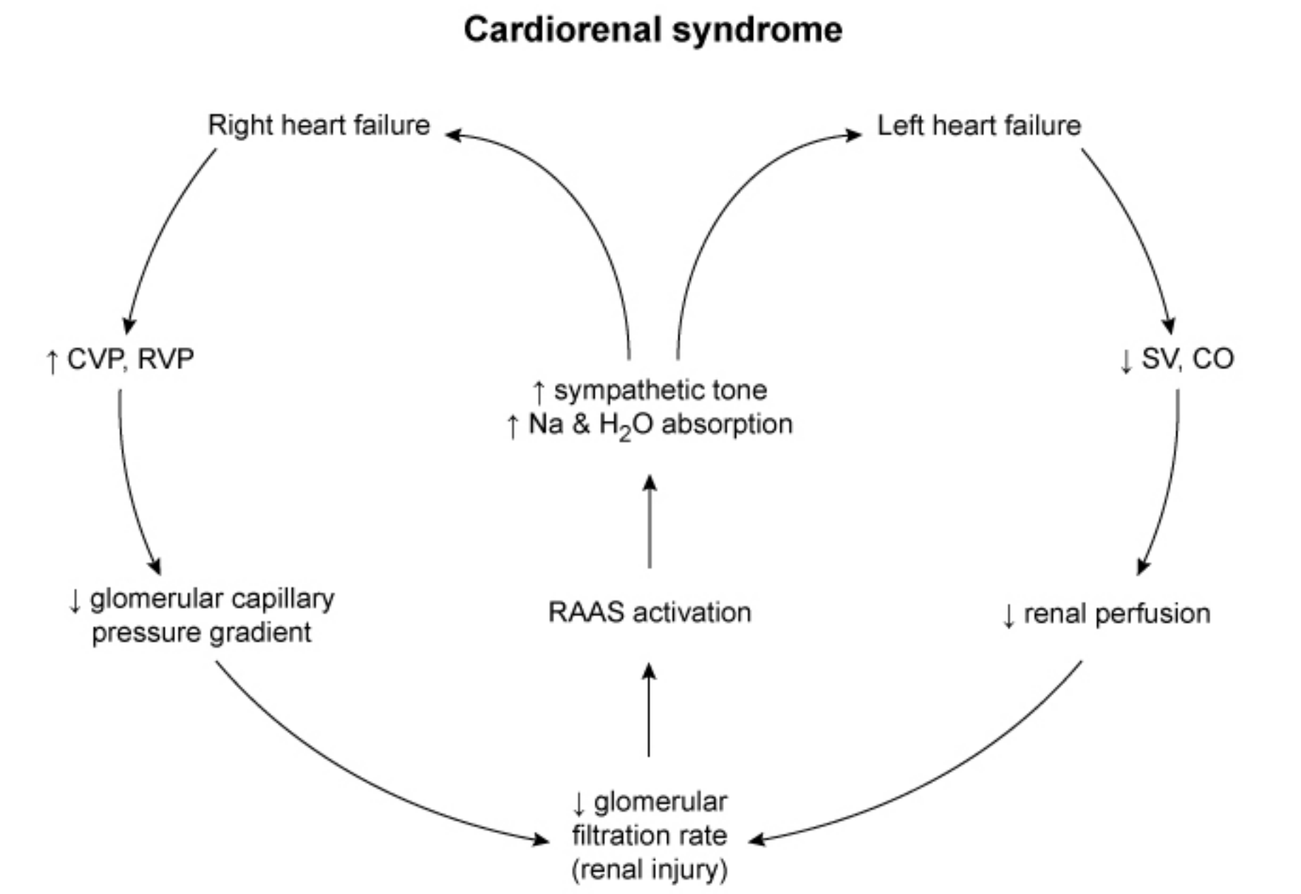
Time Spent

02/08/2020
Last Updated



CO = cardiac output; **CVP** = central venous pressure; **RAAS** = renin-angiotensin-aldosterone system; **RVP** = renal vein perfusion; **SV** = stoke volume.

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This patient with a recent upper respiratory infection has developed dyspnea, lower extremity edema, and an S3 on cardiac exam; this presentation suggests dilated cardiomyopathy with **decompensated heart failure** (CHF), likely from viral myocarditis. Renal decompensation

This patient with a recent upper respiratory infection has developed dyspnea, lower extremity edema, and an S3 on cardiac exam; this presentation suggests dilated cardiomyopathy with **decompensated heart failure** (CHF), likely from viral myocarditis. Renal decompensation (acute kidney injury or chronic kidney disease) occurs in up to 60% of patients with CHF and is often due to a complex syndrome known as **cardiorenal syndrome**.

The pathophysiology of cardiorenal syndrome is multifactorial and includes both hemodynamic alterations related to the low output state and resultant neurohormonal changes. Decreased cardiac output results in renal hypoperfusion, which triggers the following adaptations:

- Renin-angiotensin-aldosterone system (RAAS) activation, leading to **increased proximal tubular sodium reabsorption** (direct effect of angiotensin II)
- Antidiuretic hormone release, resulting in **increased free water reabsorption** in the collecting ducts
- Sympathetic nervous system activation, resulting in **systemic vasoconstriction**

In the short-term, these adaptions increase the effective arterial blood volume and maintain systemic perfusion, allowing for a relatively normal glomerular filtration rate. However, over time, widespread vasoconstriction **increases the afterload** (ie, the resistance the heart must pump against) and **ventricular overfilling** leads to decreased pump efficiency, **lowering cardiac output** and furthering renal hypoperfusion. At a certain point, the decrease in cardiac output becomes overwhelming and glomerular filtration rate begins to drop.

Characteristic laboratory findings in cardiorenal syndrome reflect **activation of the RAAS** and indicate a **prerenal** etiology, with low urine sodium and fractionated excretion of sodium (<1%). Urea is passively reabsorbed following sodium in the proximal tubule, leading to an elevated **blood urea nitrogen/creatinine ratio (>20:1)**.

(Choices A, B, and D) Decreased sodium and urea reabsorption and increased free water excretion are normal responses to elevated extracellular fluid volume. In patients with CHF, the low cardiac output leads to activation of the RAAS which inhibits these actions.

(Choices C and F) CHF is associated with decreased renal blood flow (due to low cardiac output/vasoconstriction) and increased renal venous pressure (due to volume overload), both of which act to reduce glomerular filtration rate. Elevated renal venous pressure is thought to reduce the glomerular filtration rate by increasing renal interstitial pressure and restricting blood flow through the afferent arteriole.

Educational objective:

- Antidiuretic hormone release, resulting in **increased free water reabsorption** in the collecting ducts
- Sympathetic nervous system activation, resulting in **systemic vasoconstriction**

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Educational objective:
Cardiorenal syndrome is due to hemodynamic alterations related to a low cardiac output state and maladaptive neurohormonal changes. Low cardiac output results in renal hypoperfusion, leading to activation of the renin-angiotensin-aldosterone system, antidiuretic hormone release, and increased sympathetic nervous system activity. The resultant increase in sodium and water reabsorption and systemic vasoconstriction have detrimental effects on left ventricular systolic function, further worsening cardiac output and renal perfusion.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Prerenal azotemia
Subject	System	Topic

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A 51-year-old man comes to the emergency department with sudden-onset, sharp, right flank pain; nausea; and vomiting. He has had no dysuria or hematuria. The patient has no past medical conditions and takes no daily medications. He does not use tobacco, alcohol, or illicit drugs. Temperature is normal. On examination, the patient appears to be in severe pain and cannot find a comfortable position on the bed. There is no abdominal rigidity or rebound, and no masses are palpable. Cardiopulmonary examination is normal. There is no peripheral edema. Imaging shows a 1-cm calculus in the right proximal ureter at the level of the L3 vertebra; the renal pelvis and proximal ureter are dilated, as shown in the exhibit. Which of the following is most likely increased in this patient's right kidney?

A. Bowman space oncotic pressure

B. Glomerular filtration

C. Intraglomerular capillary hydrostatic pressure

D. Tubular hydrostatic pressure

E. Tubular oncotic pressure

Submit

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A. Bowman space oncotic pressure (3%)

B. Glomerular filtration (3%)

C. Intraglomerular capillary hydrostatic pressure (9%)

✓ D. Tubular hydrostatic pressure (79%)

E. Tubular oncotic pressure (3%)

Omitted
Correct answer
D

79%
Answered correctly

02 secs
Time Spent

03/04/2020
Last Updated

Explanation

The glomerular filtration rate depends on the permeability of the capillary wall and the net ultrafiltration pressure. Net ultrafiltration pressure is a result of pressure gradients formed by Starling forces:

- **The hydrostatic pressure gradient** is the difference between the hydrostatic pressure in the intraglomerular capillaries and the Bowman

The glomerular filtration rate depends on the permeability of the capillary wall and the net ultrafiltration pressure. Net ultrafiltration pressure is a result of pressure gradients formed by Starling forces:

- **The hydrostatic pressure gradient** is the difference between the hydrostatic pressure in the intraglomerular capillaries and the Bowman space. Typically, the hydrostatic pressure in the glomerular capillaries is markedly greater than the pressure in the Bowman space, favoring filtration.
- **The oncotic pressure gradient** is the difference between the oncotic pressure in the intraglomerular capillaries and the Bowman space. Oncotic pressure is chiefly driven by large plasma proteins (eg, albumin), which do not freely filter across the glomerular capillary basement membrane due to both a size and charge barrier. Therefore, the oncotic pressure is negligible within the Bowman space, favoring absorption of fluid into the glomerular capillaries.

This patient has a kidney stone in the right ureter; the hydroureter and hydronephrosis suggest acute **urinary tract obstruction**. The resultant reflux of urine backward into the relatively noncompliant renal tubules results in **increased renal tubular hydrostatic pressure**. As the intraglomerular capillary hydrostatic pressure is unchanged, this results in a decreased hydrostatic pressure gradient leading to a reduction in glomerular filtration **(Choices B and C)**.

(Choices A and E) Oncotic pressure in the Bowman space is negligible unless glomerular disease (eg, minimal change disease, diabetic nephropathy) allows proteins to leak into the Bowman space. The renal tubules are contiguous with the Bowman space and therefore also have negligible oncotic pressure. Acute urinary tract obstruction would not affect protein filtration at the glomerulus; therefore, the oncotic pressure in these regions remains essentially unchanged.

Educational objective:
Urinary tract obstruction causes reflux of urine into the renal tubules and increased tubular hydrostatic pressure. The intraglomerular capillary hydrostatic pressure is unchanged, resulting in a decreased hydrostatic pressure gradient across the glomerular capillary wall and a reduction in glomerular filtration. Oncotic pressure is maintained by large plasma proteins which are not filtered across the glomerular capillary basement membrane; it is unaffected by a urinary tract obstruction.

Pathophysiology Renal, Urinary Systems & Electrolytes Urinary tract obstruction

- **The hydrostatic pressure gradient** is the difference between the hydrostatic pressure in the intraglomerular capillaries and the Bowman space. Typically, the hydrostatic pressure in the glomerular capillaries is markedly greater than the pressure in the Bowman space, favoring filtration.

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Educational objective:
Urinary tract obstruction causes reflux of urine into the renal tubules and increased tubular hydrostatic pressure. The intraglomerular capillary hydrostatic pressure is unchanged, resulting in a decreased hydrostatic pressure gradient across the glomerular capillary wall and a reduction in glomerular filtration. Oncotic pressure is maintained by large plasma proteins which are not filtered across the glomerular capillary basement membrane; it is unaffected by a urinary tract obstruction.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Urinary tract obstruction
Subject	System	Topic

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A 65-year-old woman is brought to the emergency department by her family due to worsening generalized weakness and lethargy. She has had no fever, chills, vomiting, or diarrhea but has been urinating frequently over the past several days. Her family also notes that the patient has lost 5 kg (11 lb) over the past month. She takes no medications and has smoked 1-2 packs of cigarettes daily for the last 40 years. On physical examination, the patient appears ill with dry mucous membranes. There are no abnormal lung sounds or heart murmurs. The abdomen is soft and nontender. Laboratory testing shows serum calcium of 14.0 mg/dL and normal serum glucose and urinalysis. Imaging studies reveal an 8-cm right lung mass with enlarged mediastinal lymph nodes but no focal bony lesions. Serum levels of which of the following substances are most likely to be elevated in this patient?

- A. 1,25-dihydroxyvitamin D
- B. ACTH
- C. Parathyroid hormone (PTH)
- D. Phosphorus
- E. PTH-related protein
- F. Thyroxine (T4)

Submit

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- A. 1,25-dihydroxyvitamin D (5%)
- B. ACTH (4%)
- C. Parathyroid hormone (PTH) (10%)
- D. Phosphorus (1%)
- ✓ E. PTH-related protein (78%)
- F. Thyroxine (T4) (0%)

Omitted
Correct answer
E

78%
Answered correctly

02 secs
Time Spent

02/29/2020
Last Updated

Explanation

Hypercalcemia of malignancy			
Cause	**Tumor type**	**Mechanism**	**Diagnostic**
PTHrP*	• **Squamous cell** • Renal & bladder • Breast & ovarian	• PTH mimic	• ↓ PTH • ↑ PTHrP
Bone metastases	• **Breast** • Multiple myeloma	• ↑ **Osteolysis**	• ↓ PTH & PTHrP • ↓ Vitamin D
1,25-dihydroxyvitamin D	• Lymphoma	• ↑ Calcium absorption	• ↓ PTH • ↑ Vitamin D

*PTHrP causes approximately 80% of malignancy-associated hypercalcemia.

PTH = parathyroid hormone; **PTHrP** = parathyroid hormone-related protein.

This patient has **symptomatic hypercalcemia**, which typically occurs in patients with a serum calcium of >12 mg/dL and manifests with weakness, neuropsychiatric symptoms (eg, lethargy), gastrointestinal symptoms (eg, constipation, nausea), or kidney stones. Severe hypercalcemia results in impairment of the concentrating capacity of the distal tubule, leading to polyuria and volume depletion. Mild hypercalcemia is usually due to benign causes (eg, primary hyperparathyroidism), but serum calcium >13 mg/dL suggests an underlying malignancy.

Humoral hypercalcemia of malignancy (HHM) is the most common cause of hypercalcemia in patients with malignancy and is due to secretion of **parathyroid hormone-related peptide** (PTHrP) by malignant cells. PTHrP closely resembles PTH at the bioactive amino-terminal region and causes increased bone resorption, decreased renal excretion of calcium, and increased renal excretion of phosphorus (leading to hypophosphatemia **[Choice D]**). However, unlike PTH, PTHrP does not significantly increase 1,25-dihydroxyvitamin D production due to structural differences after the first 13 amino acids.

HHM occurs most commonly in squamous cell (ie, lung, head and neck), renal, bladder, breast, and ovarian carcinomas. This patient's heavy

of **parathyroid hormone-related peptide** (PTHrP) by malignant cells. PTHrP closely resembles PTH at the bioactive amino-terminal region and causes increased bone resorption, decreased renal excretion of calcium, and increased renal excretion of phosphorus (leading to hypophosphatemia **[Choice D]**). However, unlike PTH, PTHrP does not significantly increase 1,25-dihydroxyvitamin D production due to structural differences after the first 13 amino acids.

HHM occurs most commonly in squamous cell (ie, lung, head and neck), renal, bladder, breast, and ovarian carcinomas. This patient's heavy smoking history, weight loss, and lung mass suggest squamous cell carcinoma of the lung. Hypercalcemia can also occur due to osteolytic bony metastasis (eg, breast cancer, multiple myeloma), but this is less common than HHM and this patient has no lytic lesions visible on imaging.

(Choice A) Hodgkin lymphoma and granulomatous diseases (eg, sarcoidosis) can express 1-alpha-hydroxylase, which increases the formation of 1,25-dihydroxyvitamin D, leading to hypercalcemia. However, this patient's large lung mass with regional lymph node enlargement is more suggestive of primary squamous cell carcinoma of the lung.

(Choice B) Ectopic ACTH secretion causes paraneoplastic Cushing syndrome, characterized by hypertension, hyperpigmentation, and proximal muscle weakness. Laboratory studies typically show hyperglycemia rather than hypercalcemia.

(Choice C) Ectopic production of PTH is a very rare cause of hypercalcemia in patients with malignancy. Patients with HHM have very low levels of PTH due to feedback suppression by hypercalcemia.

(Choice F) Thyrotoxicosis can cause mild hypercalcemia due to increased bone turnover, but severe hypercalcemia is rare, and this patient's high calcium level and lung mass is more suggestive of an underlying malignancy.

Educational objective:
Serum calcium >13 mg/dL is suggestive of an underlying malignancy. Secretion of parathyroid hormone-related protein (PTHrP), which closely resembles parathyroid hormone at the bioactive amino-terminal region, is a frequent cause of malignancy-related hypercalcemia and is commonly seen with squamous cell carcinomas (eg, lung, neck).

References

- Hypercalcemia of malignancy: an update on pathogenesis and management.

An 86-year-old man is hospitalized for a complicated hip fracture requiring surgical repair following a fall. His medical problems include prostate cancer, gout, and osteoarthritis. An indwelling urinary catheter is placed due to initial urinary retention and immobilization following the surgery. On the eighth day of hospitalization, the patient develops fever and altered mental status. After evaluation and laboratory testing, a urinary tract infection is diagnosed. Which of the following is the most effective strategy for preventing this complication?

A. Antibiotic-coated urinary catheter

B. Bladder irrigation

C. Prompt removal of catheter when no longer indicated

D. Prophylactic antibiotics

E. Routine replacement of catheter

Submit

An 86-year-old man is hospitalized for a complicated hip fracture requiring surgical repair following a fall. His medical problems include prostate cancer, gout, and osteoarthritis. An indwelling urinary catheter is placed due to initial urinary retention and immobilization following the surgery. On the eighth day of hospitalization, the patient develops fever and altered mental status. After evaluation and laboratory testing, a urinary tract infection is diagnosed. Which of the following is the most effective strategy for preventing this complication?

- A. Antibiotic-coated urinary catheter (2%)
- B. Bladder irrigation (1%)
- ✓ C. Prompt removal of catheter when no longer indicated (69%)
- D. Prophylactic antibiotics (9%)
- E. Routine replacement of catheter (17%)

Omitted
Correct answer
C

69%
Answered correctly

03 secs
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07/03/2020
Last Updated

Explanation

Catheter-associated urinary tract infection (UTI) is a frequent complication in hospitalized patients. Common symptoms are fever and pyuria. Suprapubic, flank, and costovertebral tenderness and new-onset altered mental status (delirium) can also occur. The diagnosis is based on a positive urine culture and ruling out other systemic infections (eg, pneumonia). **Duration of catheterization is the most significant risk factor for UTI**. Preventive measures include avoiding unnecessary catheterization, using sterile technique when inserting the catheter, and removing the catheter promptly when no longer needed.

Catheter-associated urinary tract infection (UTI) is a frequent complication in hospitalized patients. Common symptoms are fever and pyuria. Suprapubic, flank, and costovertebral tenderness and new-onset altered mental status (delirium) can also occur. The diagnosis is based on a positive urine culture and ruling out other systemic infections (eg, pneumonia). **Duration of catheterization is the most significant risk factor for UTI**. Preventive measures include avoiding unnecessary catheterization, using sterile technique when inserting the catheter, and removing the catheter promptly when no longer needed.

(Choice A) Antibiotic-coated urinary catheters are costly and have not shown consistent benefit in reducing the risk for UTI.

(Choice B) Bladder irrigation is reserved for patients with hematuria and blood clots and does not prevent UTI.

(Choice D) Prophylactic antibiotics have not been shown to reduce risk of catheter-associated UTI and are associated with development of antibiotic-resistant strains.

(Choice E) Although replacing an indwelling catheter can cause a short-lived reduction in urine bacterial load, it does not confer any clear benefit. Routine replacement of indwelling catheters to prevent infection is not helpful, and catheters should be changed only for specific indications (eg, active infection, obstruction).

Educational objective:
Urinary tract infections (UTIs) are common in hospitalized patients with indwelling urinary catheters. The risk for UTI can be reduced by avoiding unnecessary catheterization, using sterile technique when inserting the catheter, and removing the catheter as soon as possible.

References

- Role of duration of catheterization and length of hospital stay on the rate of catheter-related hospital-acquired urinary tract infections.
- Nosocomial urinary tract infections: A review.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Urinary tract infection
Subject	System	Topic

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Question Id: 15208

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A 76-year-old man comes to the hospital due to acute, bright red blood from the rectum. The patient had 3 large bloody bowel movements this morning, and he has felt light-headed and dizzy since. He has a history of sigmoid diverticulosis and, 2 years ago, had a similar episode of bleeding that resolved spontaneously. Temperature is 36.9 C (98.4 F), blood pressure is 90/50 mm Hg, and pulse is 110/min. Examination shows mild lethargy and delayed capillary refill. Abdominal examination shows no abnormalities. Which of the following physiologic changes in kidney function would be most likely in this patient?

A. Decreased chloride reabsorption
B. Decreased sodium reabsorption
C. Decreased urine osmolality
D. Increased renal blood flow
E. Increased tubular hydrostatic pressure
F. Increased urea reabsorption

Submit

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A 76-year-old man comes to the hospital due to acute, bright red blood from the rectum. The patient had 3 large bloody bowel movements this morning, and he has felt light-headed and dizzy since. He has a history of sigmoid diverticulosis and, 2 years ago, had a similar episode of bleeding that resolved spontaneously. Temperature is 36.9 C (98.4 F), blood pressure is 90/50 mm Hg, and pulse is 110/min. Examination shows mild lethargy and delayed capillary refill. Abdominal examination shows no abnormalities. Which of the following physiologic changes in kidney function would be most likely in this patient?

- A. Decreased chloride reabsorption (4%)
- B. Decreased sodium reabsorption (6%)
- C. Decreased urine osmolality (13%)
- D. Increased renal blood flow (6%)
- E. Increased tubular hydrostatic pressure (9%)
- ✓ F. Increased urea reabsorption (58%)

Omitted
Correct answer
F

58%
Answered correctly

02 secs
Time Spent

05/08/2020
Last Updated

Explanation

This patient has acute gastrointestinal hemorrhage resulting in **hypovolemic shock**. Clinically significant hypovolemia can occur due to acute blood loss, third-spacing (eg, pancreatitis, vasodilation in sepsis), or renal or gastrointestinal losses (eg, excessive diuresis, diarrhea). Signs of hypovolemia include dry skin with decreased turgor, dry mucous membranes, decreased urine output, and orthostatic hypotension.

This patient has acute gastrointestinal hemorrhage resulting in **hypovolemic shock**. Clinically significant hypovolemia can occur due to acute blood loss, third-spacing (eg, pancreatitis, vasodilation in sepsis), or renal or gastrointestinal losses (eg, excessive diuresis, diarrhea). Signs of hypovolemia include dry skin with decreased turgor, dry mucous membranes, decreased urine output, and orthostatic hypotension.

Changes in blood volume or osmolality are detected by sensors in the carotid, hypothalamus, atria, and kidneys and result in activation of multiple compensatory mechanisms:

- Activation of the renin-angiotensin-aldosterone system results in systemic vasoconstriction and increased aldosterone release. Aldosterone increases **sodium reabsorption** and potassium excretion in the distal tubule and collecting duct.
- The hypothalamus stimulates thirst and increases the secretion of **antidiuretic hormone** (via the posterior pituitary), which promotes water reabsorption in the collecting duct and increases systemic vasoconstriction.
- Sympathetic activity increases renal tubular sodium reabsorption, cardiac output, and systemic vasoconstriction.

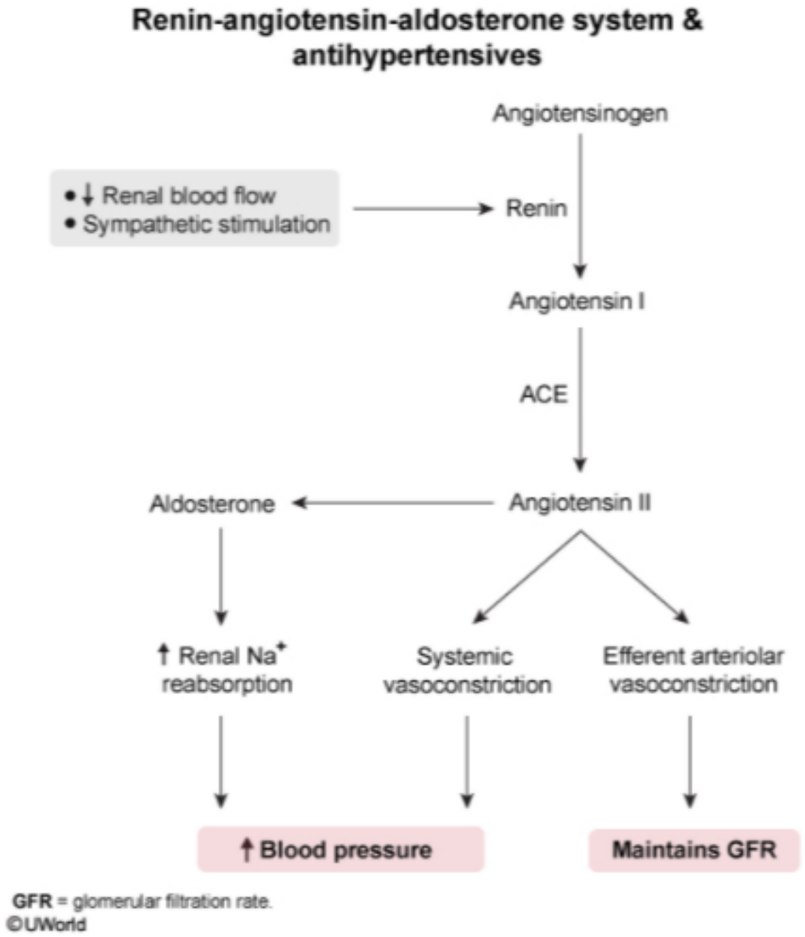
The net effect is a rapid increase in blood pressure that helps maintain tissue perfusion, while the kidney begins the slower process of restoring circulatory volume by increasing sodium, urea, and water reabsorption. **Increased urea reabsorption** is mediated by antidiuretic hormone, which increases urea permeability in the inner medullary collecting ducts. The increase in urea reabsorption accentuates the medullary concentration gradient, promoting maximal free water retention. These actions typically result in an elevated serum urea level and blood urea nitrogen/creatinine ratio (typically >20:1). Urine parameters typically show **low urine sodium concentration** (<20 mEq/L), low fractional excretion of sodium, **high urine osmolality** (>450 mOsmol/kg), and elevated urine potassium.

(Choices A, B, and C) Hypovolemia leads to increased renal salt reabsorption and elevated urine osmolality due to high serum levels of aldosterone and antidiuretic hormone.

(Choices D and E) Renal blood flow and tubular hydrostatic pressure are decreased, not increased, in patients with hypovolemia. Although activation of the renin-angiotensin-aldosterone system increases renal blood flow and tubular hydrostatic pressure in an attempt to maintain the glomerular filtration rate, these would still be lower in this patient than in a healthy patient.

Educational objective:
Compensatory mechanisms for hypovolemia include activation of the renin-angiotensin-aldosterone system and increased antidiuretic hormone

Exhibit Display



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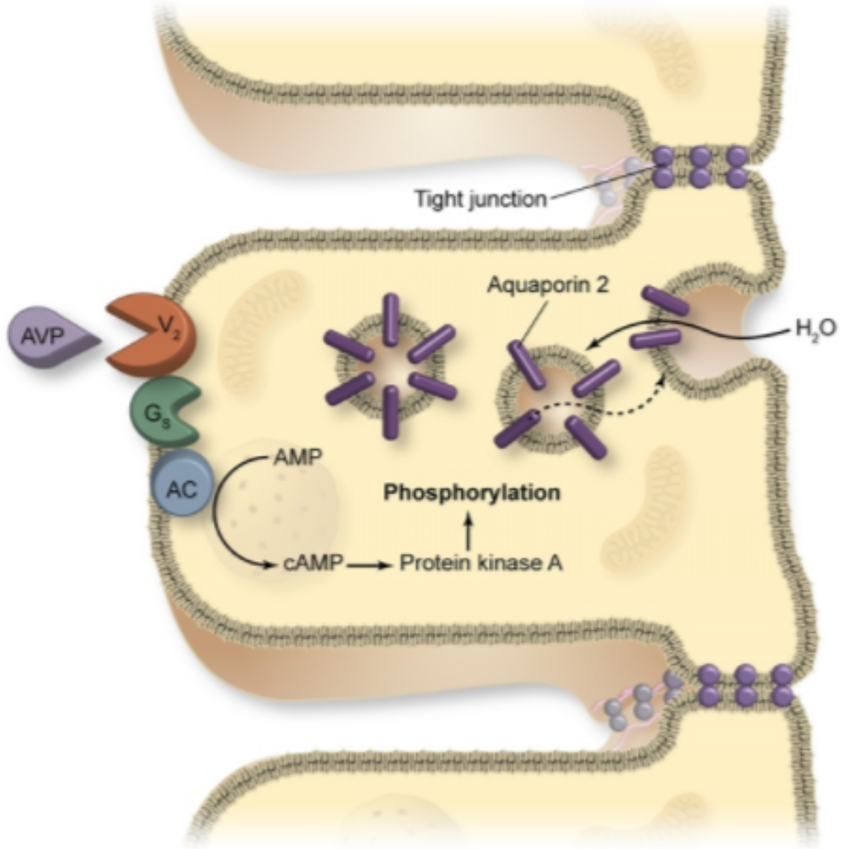
Compensatory mechanisms for hypovolemia include activation of the renin-angiotensin-aldosterone system and increased antidiuretic hormone

Exhibit Display

ADH action on collecting duct



AC = adenylyl cyclase; ADH = antidiuretic hormone; AVP = arginine vasopressin; cAMP = cyclic AMP.
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(Choices A, B, and C) Hypovolemia leads to increased renal salt reabsorption and elevated urine osmolality due to high serum levels of aldosterone and antidiuretic hormone.

(Choices D and E) Renal blood flow and tubular hydrostatic pressure are decreased, not increased, in patients with hypovolemia. Although activation of the renin-angiotensin-aldosterone system increases renal blood flow and tubular hydrostatic pressure in an attempt to maintain the glomerular filtration rate, these would still be lower in this patient than in a healthy patient.

Educational objective:
Compensatory mechanisms for hypovolemia include activation of the renin-angiotensin-aldosterone system and increased antidiuretic hormone release. This results in increased renal sodium, chloride, water, and urea reabsorption with increased potassium excretion.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Prerenal azotemia
Subject	System	Topic

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A 65-year-old man is being evaluated in the hospital. The patient was admitted 5 days ago for increasing lower extremity edema and dyspnea. Medical history is significant for obesity hypoventilation syndrome, pulmonary hypertension, and chronic lower extremity edema. Current temperature is 37.2 C (99 F), blood pressure is 110/70 mm Hg, pulse is 90/min, and respirations are 16/min. BMI is 50 kg/m^2. Laboratory results are as follows:

	Admission	Today (5th day)
Hemoglobin	13.1 g/dL	14.5 g/dL
Blood glucose	98 mg/dL	90 mg/dL
Blood urea nitrogen	24 mg/dL	64 mg/dL
Serum creatinine	1.2 mg/dL	2.1 mg/dL
Urinalysis		negative for protein, red blood cells, white blood cells, and casts
Urine sodium		10 mEq/L

Which of the following is the most likely cause of the laboratory abnormalities in this patient?

- A. Diuretic therapy
- B. Interstitial nephritis
- C. Osmotic diuresis
- D. Renal artery stenosis
- E. Tubular necrosis
- F. Ureteral compression

temperature is 37.2 °C (99 °F), blood pressure is 110/70 mm Hg, pulse is 90/min, and respirations are 16/min. BMI is 30 kg/m². Laboratory results are as follows:

	Admission	Today (5th day)
Hemoglobin	13.1 g/dL	14.5 g/dL
Blood glucose	98 mg/dL	90 mg/dL
Blood urea nitrogen	24 mg/dL	64 mg/dL
Serum creatinine	1.2 mg/dL	2.1 mg/dL
Urinalysis		negative for protein, red blood cells, white blood cells, and casts
Urine sodium		10 mEq/L

Which of the following is the most likely cause of the laboratory abnormalities in this patient?

- A. Diuretic therapy (42%)
- B. Interstitial nephritis (8%)
- C. Osmotic diuresis (7%)
- D. Renal artery stenosis (20%)
- E. Tubular necrosis (13%)
- F. Ureteral compression (7%)

Omitted
Correct answer

42%
Answered correctly

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Time Spent

05/08/2020
Last Updated

Explanation

Manifestations of hypovolemia	
Etiology	• Renal, gastrointestinal, or skin loss • Hemorrhage & third spacing (eg, pancreatitis, sepsis)
Clinical examination	• Dry mucous membranes • Dry skin; decreased turgor • Orthostatic hypotension, low-normal blood pressure
Laboratory studies	• ↑ BUN/creatinine ratio (>20:1) • Hemoconcentration (↑ albumin, ↑ hemoglobin, ↑ uric acid) • ↓ Urine sodium & FENa (<1%) • ↑ Urine specific gravity (>1.015), ↑ urine osmolality (>450 mOsm/kg)

BUN = blood urea nitrogen; **FENa** = fractional excretion of sodium.

This patient has volume overload due to right-sided heart failure from pulmonary hypertension; he was most likely treated with diuretics to improve his volume status. However, laboratory results on day 5 demonstrate an abrupt decrease in renal function with **low urine sodium** and an **elevated BUN/creatinine ratio** (prerenal azotemia). In association with a **normal urinalysis**, this presentation suggests volume depletion from the **excessive use of diuretics**.

Excessive diuresis can cause renal hypoperfusion and activation of the renin-angiotensin-aldosterone system (RAAS), which increases solute and water reabsorption by the kidney in an attempt to restore intravascular volume. As a result, laboratory studies will show **low urine sodium** (<20 mEq/L) and low fractional excretion of sodium (**FENa <1%**). Urea reabsorption is also increased in the collecting ducts, resulting in an **increased BUN/creatinine ratio** (>20:1). Elevated urine osmolality (>450 mOsm/kg) and urine specific gravity (>1.015) reflect **concentrated urine**. Evidence of hemoconcentration (eg, increased hemoglobin, albumin, uric acid levels) is also common in volume depleted patients.

(Choice B) Interstitial nephritis is characterized by acute kidney injury following exposure to a new medication. Diuretics are a common cause of

This patient has volume overload due to right-sided heart failure from pulmonary hypertension; he was most likely treated with diuretics to improve his volume status. However, laboratory results on day 5 demonstrate an abrupt decrease in renal function with **low urine sodium** and an **elevated BUN/creatinine ratio** (prerenal azotemia). In association with a **normal urinalysis**, this presentation suggests volume depletion from the **excessive use of diuretics**.

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(Choice B) Interstitial nephritis is characterized by acute kidney injury following exposure to a new medication. Diuretics are a common cause of interstitial nephritis, but urinalysis typically shows pyuria, white blood cell casts, and eosinophils.

(Choice C) Osmotic diuresis can cause hypovolemia with low urine sodium but most commonly occurs due to hyperglycemia (eg, uncontrolled diabetes). This patient's blood glucose is normal.

(Choice D) Renal artery stenosis causes chronic activation of the RAAS. Patients can develop prerenal failure, but this typically occurs after initiation of an ACE inhibitor rather than a diuretic, and patients are typically hypertensive at baseline.

(Choice E) Acute tubular necrosis can be seen in patients with renal ischemia, which can occur in severe hypovolemia; however, muddy brown casts are seen on urinalysis. Laboratory results also demonstrate an intrinsic renal injury pattern (ie, BUN/creatinine ratio ~10:1, FENa >2%) due to impaired tubular function.

(Choice F) Ureteral compression can cause unilateral renal obstruction, but AKI typically develops only with bilateral ureteral or bladder outflow obstruction (eg, prostatic hypertrophy). Patients develop significant oliguria or anuria, and pain or a sensation of incomplete voiding is common. Urine studies (ie, sodium, FENa, osmolality) are variable.

Educational objective:
Hypovolemia (eg, excessive diuresis) can cause acute kidney injury due to reduced renal blood flow (prerenal azotemia). Urine sodium and fractional excretion of sodium levels are low, and the BUN/creatinine ratio is elevated. In severe cases, acute tubular necrosis can occur and

Evidence of hemoconcentration (eg, increased hemoglobin, albumin, uric acid levels) is also common in volume depleted patients.

(Choice B) Interstitial nephritis is characterized by acute kidney injury following exposure to a new medication. Diuretics are a common cause of interstitial nephritis, but urinalysis typically shows pyuria, white blood cell casts, and eosinophils.

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Educational objective:
Hypovolemia (eg, excessive diuresis) can cause acute kidney injury due to reduced renal blood flow (prerenal azotemia). Urine sodium and fractional excretion of sodium levels are low, and the BUN/creatinine ratio is elevated. In severe cases, acute tubular necrosis can occur and cause an intrinsic renal injury pattern (ie, high urine sodium, normal BUN/creatinine ratio) with muddy brown casts on urinalysis.

References

- Analysis of the prerenal contributions to acute kidney injury.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Prerenal azotemia
Subject	System	Topic

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A 2-year-old child is brought to his pediatrician because of failure to thrive and polyuria. He is found to have glucosuria on urinalysis, although his serum glucose is within normal limits. What renal defect is responsible for his condition?

A. Necrosis of the renal papilla

B. Inflammation and fibrosis of the interstitium

C. Increased permeability of the glomerular membrane

D. Defect in proximal tubular reabsorption

E. Multiple cysts in the renal parenchyma

Submit

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A. Necrosis of the renal papilla (0%)

B. Inflammation and fibrosis of the interstitium (0%)

C. Increased permeability of the glomerular membrane (10%)

✓ D. Defect in proximal tubular reabsorption (85%)

E. Multiple cysts in the renal parenchyma (3%)

Omitted
Correct answer
D

85%
Answered correctly

02 secs
Time Spent

03/09/2020
Last Updated

Explanation

Glucose, bicarbonate, amino acids, calcium, and phosphate are normally filtered by the glomerulus and reabsorbed by the proximal tubule. When **proximal tubular transport** is defective (as in Fanconi syndrome), these substances appear in the urine despite being present at normal concentrations in serum. The classic signs and symptoms of **Fanconi syndrome** are caused by the loss of various substances in the urine.Fanconi syndrome can be inherited through autosomal dominant, autosomal recessive, or X-linked mechanisms.

Clinical manifestations such as polyuria, polydipsia, and failure to thrive tend to occur in the first years of life. Increased calcium loss in urine leads to calcium mobilization from bones, which causes severe rickets. Hypercalciuria predisposes to nephrolithiasis. Glucosuria and low urinary pH trigger frequent and severe urinary tract infections. Urinalysis reveals the presence of glucose, amino acids, bicarbonate, calcium and phosphate

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(Choice A) Renal papillary necrosis manifests with flank pain, hematuria, and the excretion of tissue fragments in urine. Renal papillary necrosis is associated with sickle cell disease, diabetes mellitus, and urinary tract obstruction.

(Choice B) Interstitial inflammation and fibrosis is characteristic of chronic interstitial nephritis. This condition usually occurs in adults as a result of chronic pyelonephritis, analgesic nephropathy, or metabolic abnormalities. Polyuria, nocturia, and urinary frequency are common. Glucosuria is not seen, however.

(Choice C) Increased permeability of the glomerular membrane is characteristic of numerous glomerular disorders that manifest with nephrotic syndrome or nephritic syndrome. These disorders do not affect proximal tubular reabsorption.

(Choice E) Multiple cysts within the renal parenchyma are seen in infantile polycystic kidney disease (ARPKD), which leads to oligohydramnios in utero. Affected children are usually born with signs of Potter syndrome (eg, pulmonary hypoplasia, flat facies, limb deformities) and can die of respiratory failure during the first months of life.

Educational objective:
Fanconi syndrome is an inherited disorder of proximal tubular transport. Glucose, bicarbonate, calcium, phosphate, and amino acids are lost, leading to a number of metabolic abnormalities. The classic clinical presentation includes failure to thrive, polyuria, polydipsia, and rickets.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Fanconis syndrome
Subject	System	Topic

A 6-week-old term boy is brought to the office due to increased fussiness and poor weight gain. The patient has several wet diapers per day. His anterior fontanelle is flat and mucous membranes are dry. Laboratory results include the following:

Sodium	148 mEq/L
Potassium	3.5 mEq/L
Antidiuretic hormone	increased

Urinalysis shows a specific gravity of 1.002. Which of the following is the most appropriate treatment for this patient's condition?

- A. Desmopressin
- B. Hydrochlorothiazide
- C. Hydrocortisone
- D. Insulin
- E. Salt tablets

Submit

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Potassium	3.5 mEq/L
Antidiuretic hormone	increased

Urinalysis shows a specific gravity of 1.002. Which of the following is the most appropriate treatment for this patient's condition?

A. Desmopressin (25%)
✓ B. Hydrochlorothiazide (49%)
C. Hydrocortisone (11%)
D. Insulin (7%)
E. Salt tablets (6%)

Omitted
Correct answer
B

49%
Answered correctly

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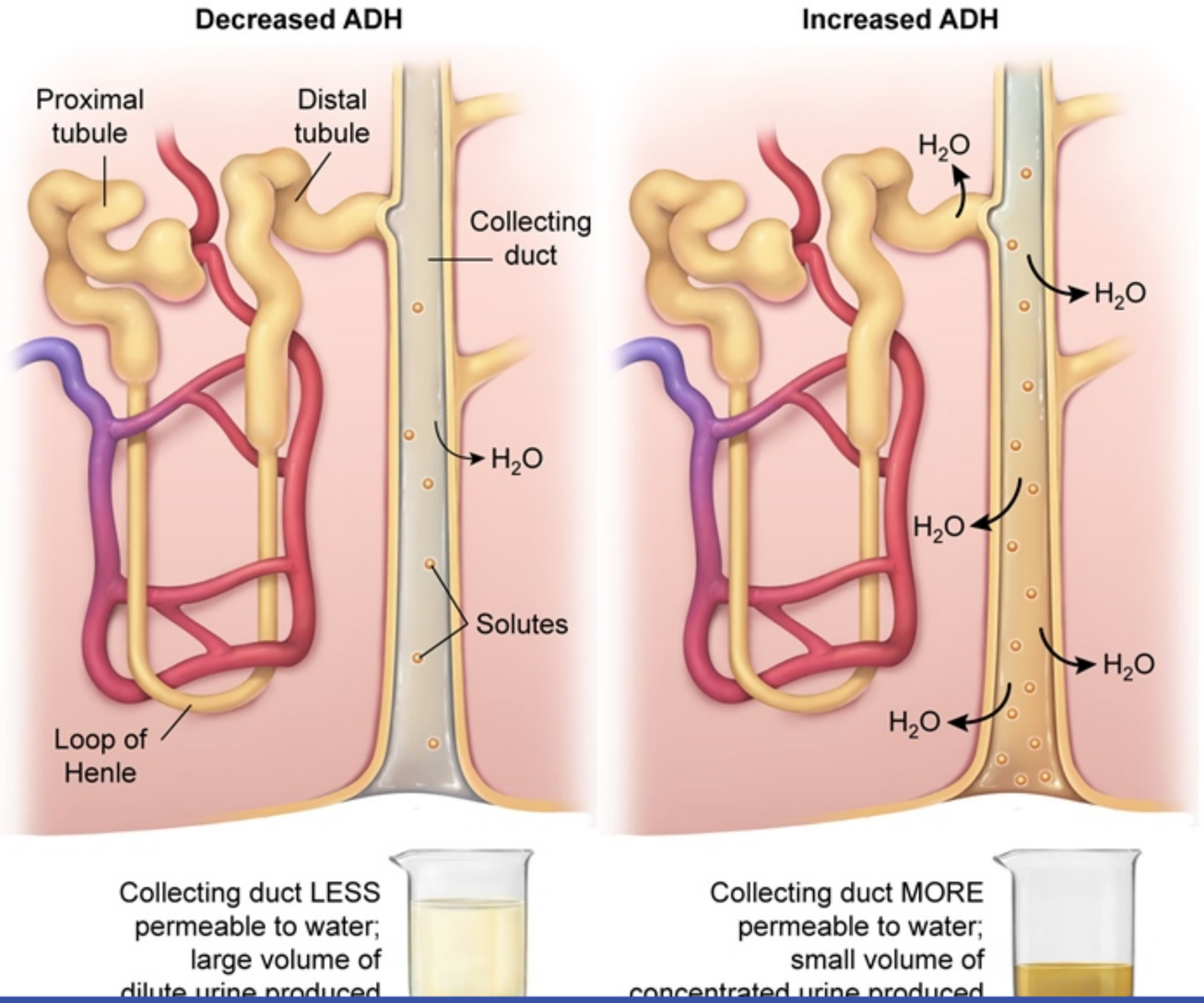
Time Spent

02/19/2020
Last Updated

Explanation

Effects of ADH on kidney function



This **dehydrated infant** (eg, flat fontanelle, dry mucous membranes, hypernatremia) is inappropriately producing **dilute urine** (eg, low urine specific gravity [<1.006]) **in large quantities** (eg, several wet diapers daily) despite having **high levels of ADH**, which is consistent with **nephrogenic diabetes insipidus (NDI)**. NDI is caused by resistance to **antidiuretic hormone** (ADH, or vasopressin) within the renal collecting ducts. Although NDI in adults is commonly due to medications (eg, lithium), in children, it is typically due to congenital mutations involving the vasopressin (V2) receptor or aquaporin 2 channel.

ADH is secreted when serum osmolality is high (eg, water deprivation) or extracellular volume is low (eg, dehydration). Normally, ADH increases water reabsorption in the renal collecting ducts, which increases urinary concentration (eg, high urine osmolality and specific gravity) and lowers serum sodium, serum osmolality, and urinary volume.

Infants with NDI cannot freely replace ongoing water losses, and early diagnosis and treatment is essential for preventing associated mental and physical growth retardation. Treatment aims to minimize urinary water loss and includes **frequent water supplementation** and, paradoxically, **thiazide administration** (eg, hydrochlorothiazide). Thiazides appear to **reduce renal water losses** in NDI by inducing a mild volume depletion that increases sodium and water reabsorption in the proximal tubule. This decreases the total amount of water delivered to the collecting ducts, allowing for better retention of supplemental water.

(Choice A) Desmopressin (an ADH analog) is used to treat central diabetes insipidus, a disorder caused by deficient ADH secretion by the hypothalamus and posterior pituitary. Central diabetes insipidus is associated with low, rather than high, ADH levels.

(Choice C) Hydrocortisone can be used to treat adrenal insufficiency, which may also present with hypovolemia and high ADH levels. However, renal ADH response is intact; therefore, hyponatremia and high urine specific gravity would be expected

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(Choice D) Severe hyperglycemia from diabetes mellitus can lead to polyuria and dehydration; however, increased urinary glucose would cause high urine specific gravity and urine osmolality.

(Choice E) Salt tablets can treat the syndrome of inappropriate ADH, which is associated with hyponatremia and high urine specific gravity.

Educational objective:
Nephrogenic diabetes insipidus is characterized by polyuria, dilute urine (low urine specific gravity), hypernatremia, and high antidiuretic hormone. Treatment includes thiazide diuretics and replacement of water losses.

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Educational objective:
Nephrogenic diabetes insipidus is characterized by polyuria, dilute urine (low urine specific gravity), hypernatremia, and high antidiuretic hormone. Treatment includes thiazide diuretics and replacement of water losses.

References

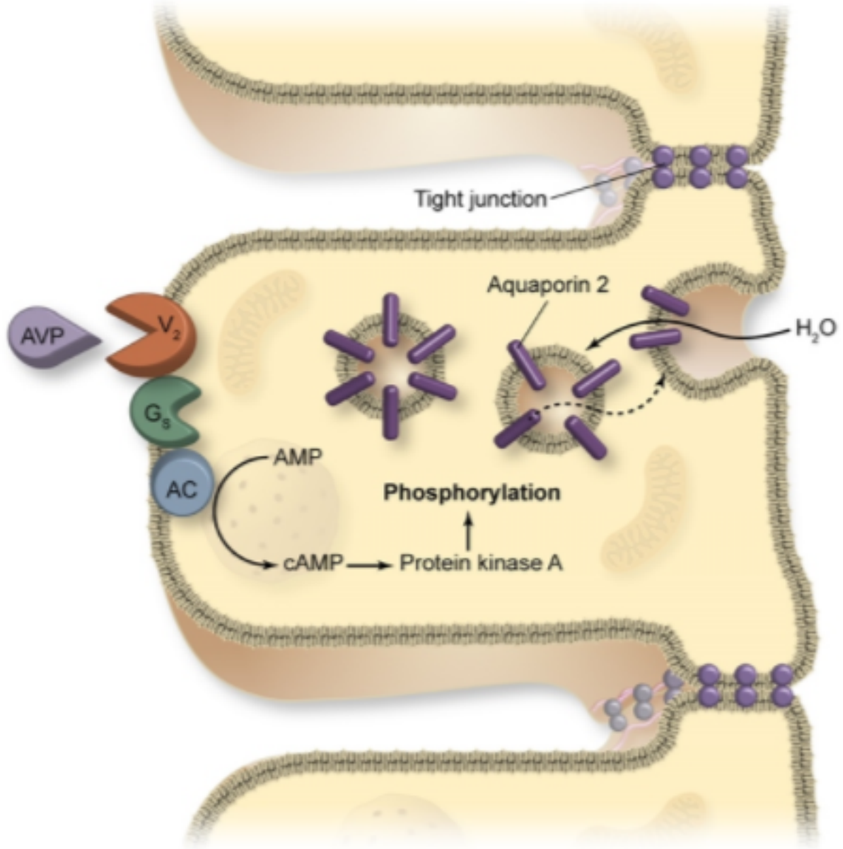
- Paradoxical antidiuretic effect of thiazides in diabetes insipidus: another piece in the puzzle.
- Management of diabetes insipidus in children.

dilute urine produced

concentrated urine produced

Exhibit Display

ADH action on collecting duct



AC = adenylyl cyclase; **ADH** = antidiuretic hormone; **AVP** = arginine vasopressin; **cAMP** = cyclic AMP.

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(Choice E) Salt tablets can treat the syndrome of inappropriate ADH, which is associated with hyponatremia and high urine specific gravity.

A 60-year-old man comes to the office due to persistent cough for the past several weeks. He reports producing minimal sputum that recently has contained occasional specks of blood. The patient also has anorexia and has lost 7 kg (15.4 lb) over the past 2 months. He has no previous medical conditions and takes no medications. The patient has smoked a pack of cigarettes daily for 40 years and drinks alcohol on social occasions. Temperature is 37.1 C (98.7 F), blood pressure is 130/80 mm Hg, pulse is 72/min, and respirations are 16/min. On physical examination, respirations are unlabored, and there are occasional wheezes on the left side. The remainder of the examination shows no abnormalities. A chest x-ray reveals a hilar mass with adenopathy on the left side. Laboratory results demonstrate a decreased serum sodium level. Which of the following additional laboratory abnormalities are most likely to be present in this patient?

	Serum osmolality	Urine osmolality	Urine sodium
A.	High	High	Normal
B.	High	Low	Normal
C.	Low	High	High
D.	Low	High	Low
E.	Low	Low	Low

Submit

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	Serum osmolality	Urine osmolality	Urine sodium
A. (0%)	High	High	Normal
B. (3%)	High	Low	Normal
✓ C. (69%)	Low	High	High
D. (22%)	Low	High	Low
E. (3%)	Low	Low	Low

Omitted
Correct answer
C

69%
Answered correctly

03 secs
Time Spent

03/14/2020
Last Updated

Conditions associated with abnormal sodium levels			
Disorder	**Serum sodium**	**Serum osmolality**	**Urine osmolality**
Diabetes insipidus	High/normal	High	Low
Primary polydipsia	Low	Low	Low
Diabetes mellitus*	Low	High	High
SIADH	Low	Low	High

*In the setting of marked hyperglycemia.

SIADH = syndrome of inappropriate secretion of antidiuretic hormone.

This patient with a significant smoking history, cough, weight loss, and left-sided **hilar lung mass** with adenopathy likely has lung cancer. He also has new **hyponatremia**. Certain tumors (eg, small cell lung carcinoma, head and neck cancer) can ectopically produce antidiuretic hormone (ADH), which can lead to hyponatremia due to the **syndrome of inappropriate secretion of ADH** (SIADH).

ADH secretion from the posterior pituitary is normally stimulated by high serum osmolality (eg, water deprivation) or low extracellular volume (eg, dehydration). Increased ADH leads to water reabsorption in the renal collecting ducts, lowering serum osmolality and suppressing further ADH secretion. However, in SIADH, excessive uncontrolled ADH secretion occurs, causing the following changes:

- **Hyponatremia** and **low serum osmolality** as a result of excess water retention
- **Concentrated urine** with **high urine osmolality** as a result of impaired renal water excretion
- **High urine sodium** caused by increased secretion of natriuretic peptides (eg, brain natriuretic peptides) **(Choice D)**

Patients with SIADH are typically **euvolemic** (eg, absent jugular venous distension, normotension). Initially, increased reabsorption of water in SIADH may cause a transient volume expansion; however, subsequent natriuresis (sodium and water excretion) restores the extracellular volume to normal.

- **Hyponatremia** and **low serum osmolality** as a result of excess water retention
- **Concentrated urine** with **high urine osmolality** as a result of impaired renal water excretion
- **High urine sodium** caused by increased secretion of natriuretic peptides (eg, brain natriuretic peptides) **(Choice D)**

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(Choice A) High serum osmolality and high urine osmolality (concentrated urine) can be seen in severe hyperglycemia (eg, diabetic ketoacidosis). High urine osmolality and polyuria results from increased glucose excretion in the urine (osmotic diuresis); dilutional hyponatremia can also occur due to the glucose-driven osmotic pull of water into the extracellular space.

(Choice B) High serum osmolality with low urine osmolality (dilute urine) can be seen in diabetes insipidus, a condition characterized by polyuria and excessive urinary water losses. However, diabetes insipidus is associated with a high or high/normal serum sodium, rather than this patient's hyponatremia. This patient also has no history of polyuria.

(Choice E) Low serum osmolality and low urine osmolality are characteristic of primary polydipsia, a disorder caused by excessive water intake. This disorder can be due to CNS disorders or psychotropic medications and is also associated with hyponatremia (ie, hypotonic hyponatremia). However, ADH levels are low, rather than increased, and patients often have polyuria. This patient has no history of excessive water intake or polyuria.

Educational objective:
Ectopic production of antidiuretic hormone (ADH) from malignancy can lead to the syndrome of inappropriate ADH secretion, a condition of impaired urinary water excretion. This condition manifests with low serum osmolality, hyponatremia, high urine osmolality, and high urine sodium.

References

- Syndrome of inappropriate antidiuretic hormone secretion: Revisiting a classical endocrine disorder.

Pathophysiology	Renal, Urinary Systems & Electrolytes	SIADH
Subject	System	Topic

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Item 21 of 26
Question Id: 956

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A 35-year-old man who works as a nurse at a local hospital is brought to the emergency department due to confusion and lethargy. His temperature is 36.7 C (98 F), blood pressure is 86/48 mm Hg, pulse is 120/min, and respirations are 12/min. Arterial blood gas results show pH 7.54, $PaCO_2$ 49 mm Hg, and PaO_2 85 mm Hg. Which of the following laboratory studies would be the most useful in determining the cause of this patient's acid-base abnormality?

A. Serum ketones
B. Serum osmolality
C. Serum sodium
D. Urine chloride
E. Urine glucose

Submit

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A. Serum ketones (8%)

B. Serum osmolality (23%)

C. Serum sodium (21%)

✓ D. Urine chloride (42%)

E. Urine glucose (3%)

Omitted
Correct answer
D

42%
Answered correctly

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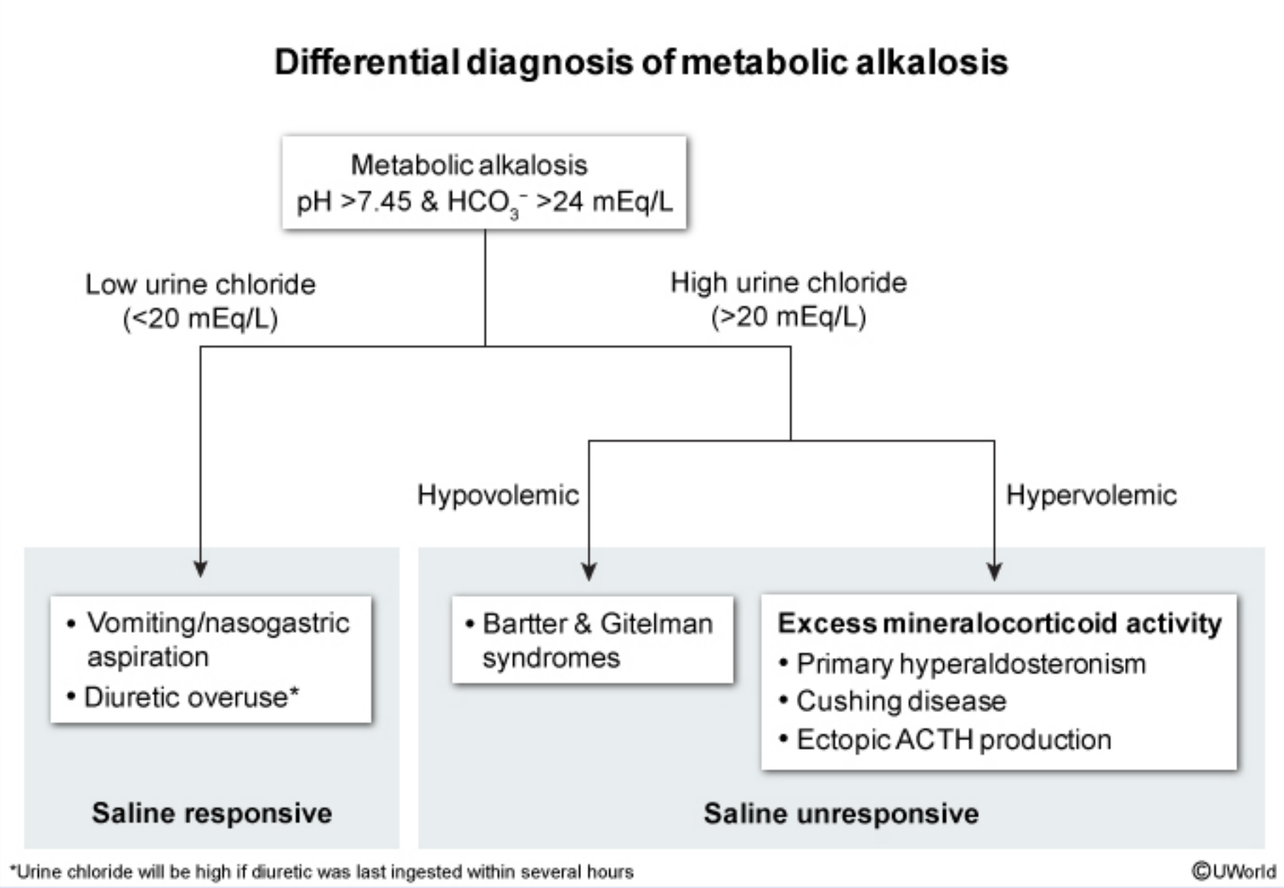
04/15/2020
Last Updated

Explanation

Differential diagnosis of metabolic alkalosis

Metabolic alkalosis
pH >7.45 & HCO_3^- >24 mEq/L



This patient's arterial pH >7.45 is consistent with alkalemia. The $PaCO_2$ is elevated (>40 mm Hg), indicating a respiratory acidosis, which does not explain the alkalemia. Therefore, **primary metabolic alkalosis with respiratory compensation** is most likely present. When the etiology of metabolic alkalosis is unknown, assessment of **volume status** and measurement of **urine chloride** can be helpful.

Because low Cl^- impairs renal excretion of HCO_3^-, total body **chloride depletion** often plays an important role in the pathogenesis of metabolic alkalosis. Etiologies of metabolic alkalosis that involve temporary chloride depletion (**hypovolemia**) will demonstrate **low urine chloride** and are

*Urine chloride will be high if diuretic was last ingested within several hours

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Because low Cl^- impairs renal excretion of HCO_3^-, total body **chloride depletion** often plays an important role in the pathogenesis of metabolic alkalosis. Etiologies of metabolic alkalosis that involve temporary chloride depletion (**hypovolemia**) will demonstrate **low urine chloride** and are amenable to treatment with Cl^- repletion (**saline responsive**). These etiologies include:

- **Nasogastric suctioning** or **severe vomiting**, which involve loss of H^+ and Cl^- (ie, hydrochloric acid) from the stomach.
- **Loop or thiazide diuretic overuse**, which involve loss of Cl^- and retention of HCO_3^- by the kidneys. Of note, urine chloride will be high with recent use but drops to low levels once the diuretic effect wanes.

Metabolic alkalosis can also occur in the absence of significant chloride depletion. Conditions of **mineralocorticoid excess** (eg, primary hyperaldosteronism) cause metabolic alkalosis primarily due to aldosterone-mediated H^+ loss from the kidneys. These patients have **hypervolemia** (eg, hypertension), resulting in a pressure natriuresis with **high urine chloride** levels; the metabolic alkalosis does not correct with Cl^- repletion (**saline unresponsive**) due to the persistent mineralocorticoid effect.

Certain renal tubular channelopathies (eg, Bartter and Gitelman syndromes) represent a special case. Although affected patients are hypovolemic and total body chloride is low, high urine chloride is present because the defect persistently impairs renal Cl- reabsorption.

(Choices A and E) Assessment of serum ketones and urine glucose is helpful in the evaluation of diabetic ketoacidosis as a cause of metabolic acidosis. However, this patient has metabolic alkalosis.

(Choices B and C) Intravascular volume depletion can also contribute to metabolic alkalosis by increasing renal bicarbonate reabsorption. However, *serum sodium concentration* is an indication of the relative amounts of total body sodium and total body water; it provides *little information about overall volume status* (ie, hypo- or hypernatremia can occur with hypovolemia, euvolemia, or hypervolemia). Serum osmolality usually reflects serum sodium concentration unless high levels of other osmotically active substances are present (eg, glucose, ethanol); like serum sodium, it cannot be used to reliably differentiate hypovolemia from hypervolemia.

Educational objective:

recent use but drops to low levels once the diuretic effect wanes.

Metabolic alkalosis can also occur in the absence of significant chloride depletion. Conditions of **mineralocorticoid excess** (eg, primary hyperaldosteronism) cause metabolic alkalosis primarily due to aldosterone-mediated H^+ loss from the kidneys. These patients have **hypervolemia** (eg, hypertension), resulting in a pressure natriuresis with **high urine chloride** levels; the metabolic alkalosis does not correct with Cl^- repletion (**saline unresponsive**) due to the persistent mineralocorticoid effect.

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Educational objective:
Total body chloride depletion is often important in the pathophysiology of metabolic alkalosis. Measurement of urine chloride can be helpful in determining the underlying etiology.

References

- Metabolic alkalosis.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Metabolic alkalosis
Subject	System	Topic

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• Vomiting/nasogastric aspiration

• Bartter & Gitelman syndromes

Excess mineralocorticoid activity

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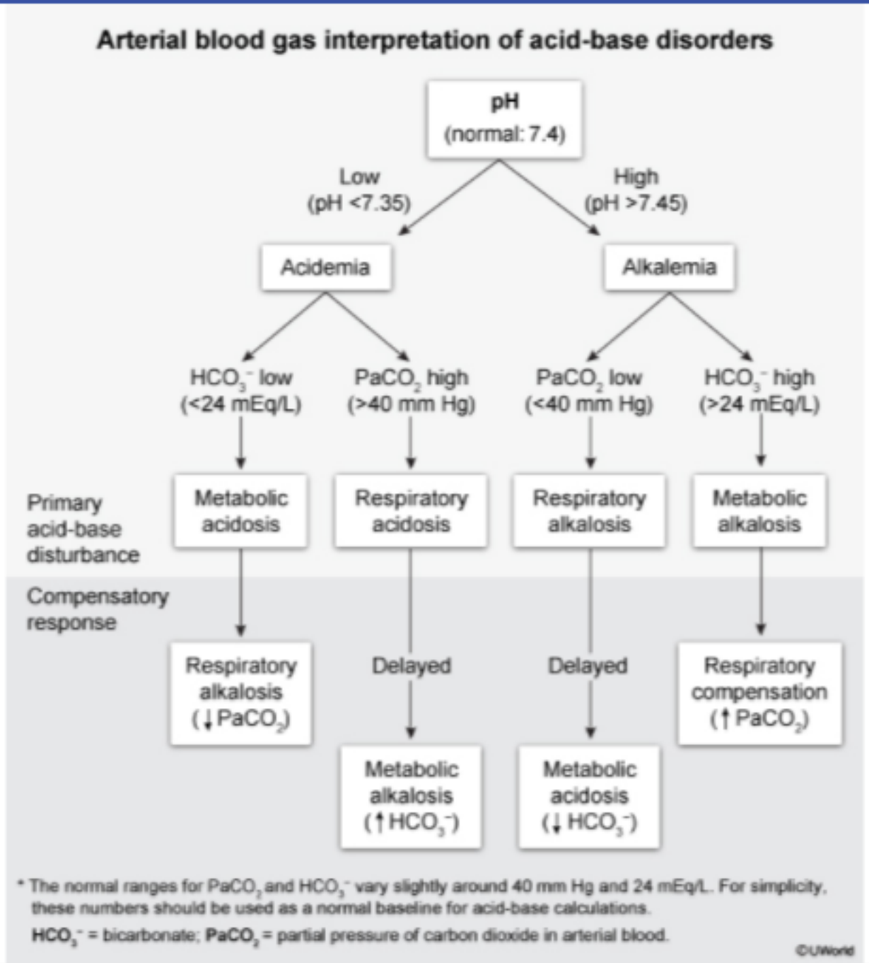

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• Vomiting/nasogastric aspiration

• Bartter & Gitelman syndromes

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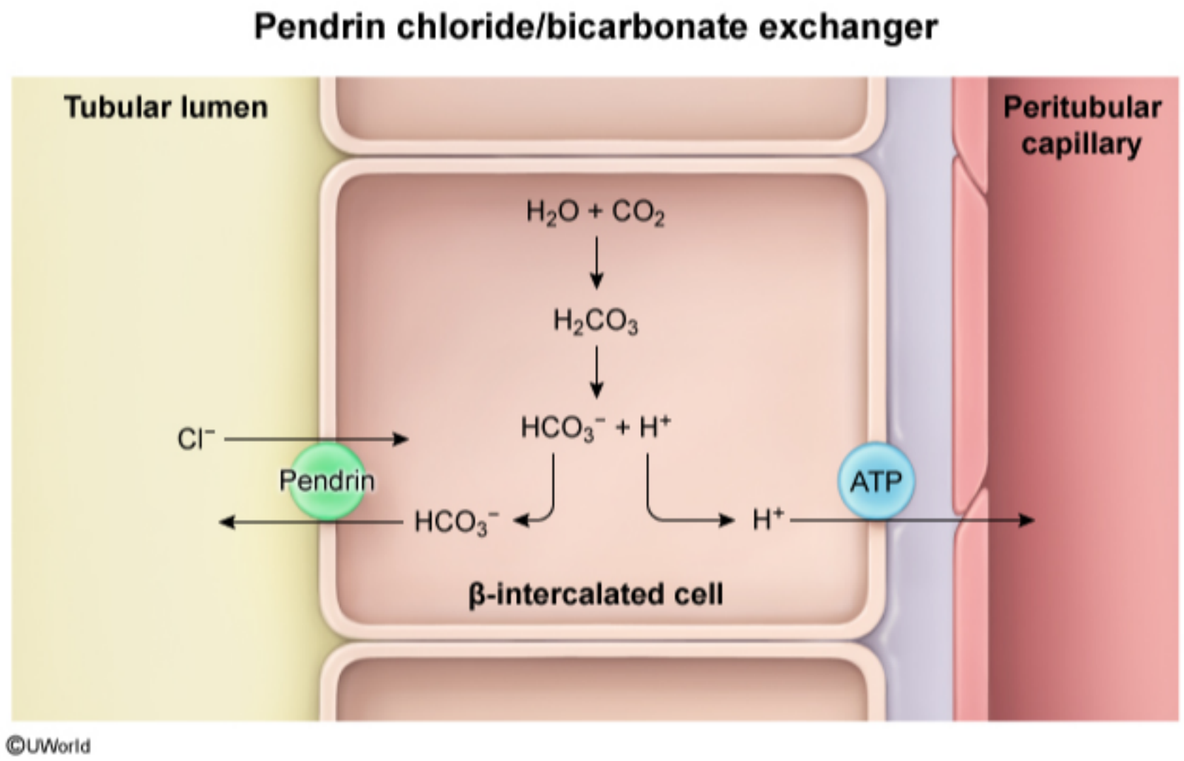

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(Choices B and C) Intravascular volume depletion can also contribute to metabolic alkalosis by increasing renal bicarbonate reabsorption.

A 45-year-old man comes to the office for an annual medical visit. The patient has had prediabetes for the last 2 years. He feels well and takes no medications but has gained weight since his last visit a year ago. The patient has a strong family history of type 2 diabetes mellitus. Blood pressure is 124/78 mm Hg and BMI is 32 kg/m^2. Laboratory results show a fasting blood glucose of 157 mg/dL and serum creatinine of 0.7 mg/dL. Hemoglobin A1c is 7.4%. Urine assay shows no detectable albuminuria. Which of the following renal changes is most likely present in this patient at this time?

- A. Decreased peritubular capillary oncotic pressure
- B. Decreased intraglomerular capillary pressure
- C. Glomerular atrophy
- D. Increased glomerular filtration rate
- E. Increased oncotic pressure in Bowman's space

Submit

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- A. Decreased peritubular capillary oncotic pressure (6%)
- B. Decreased intraglomerular capillary pressure (7%)
- C. Glomerular atrophy (3%)
- ✓ D. Increased glomerular filtration rate (55%)
- E. Increased oncotic pressure in Bowman's space (26%)

Omitted
Correct answer
D

55%
Answered correctly

02 secs
Time Spent

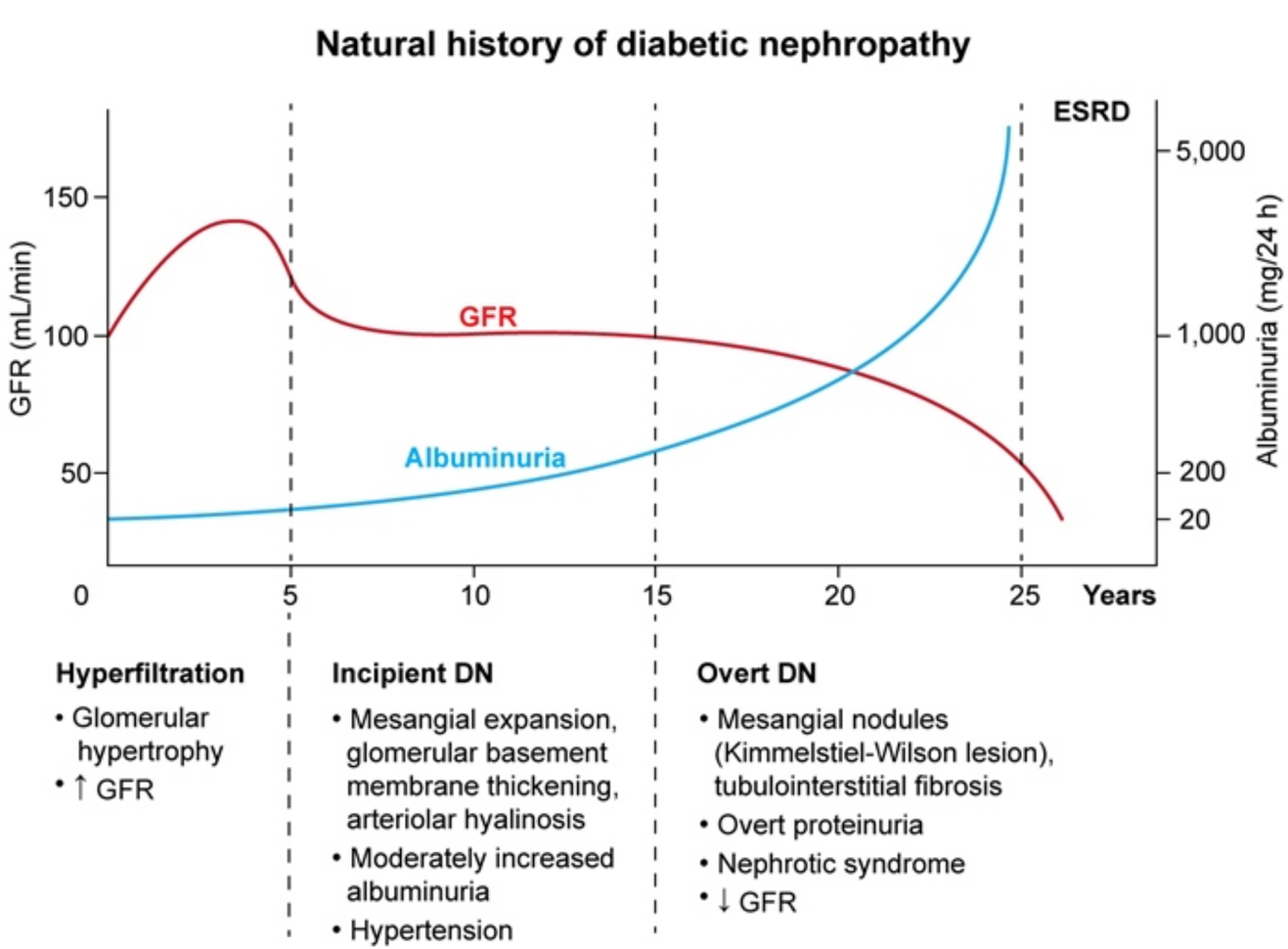
05/05/2020
Last Updated

Explanation

This patient has type 2 diabetes mellitus, confirmed by elevated blood glucose and hemoglobin A1c. **Diabetic nephropathy** can occur with any form of diabetes mellitus and is the most common cause of end-stage renal disease in the United States.

One of the earliest derangements that contributes to the pathogenesis of diabetic nephropathy is an **increase in the filtered glucose** load. This

Explanation



DN = diabetic nephropathy; **ESRD** = end-stage renal disease; **GFR** = glomerular filtration rate.
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This patient has type 2 diabetes mellitus, confirmed by elevated blood glucose and hemoglobin A1c. **Diabetic nephropathy** can occur with any

This patient has type 2 diabetes mellitus, confirmed by elevated blood glucose and hemoglobin A1c. **Diabetic nephropathy** can occur with any form of diabetes mellitus and is the most common cause of end-stage renal disease in the United States.

One of the earliest derangements that contributes to the pathogenesis of diabetic nephropathy is an **increase in the filtered glucose** load. This increases sodium resorption in the proximal tubule by the sodium glucose cotransporter, leading to decreased sodium and fluid delivery to the macula densa and subsequent activation of the tubuloglomerular autoregulation system. Subsequent dilation of the afferent arterioles and constriction of the efferent arterioles increases intraglomerular capillary pressure, resulting in an **increased glomerular filtration rate** (hyperfiltration) and glomerular hypertrophy **(Choices B and C)**.

Although the increased filtration rate appropriately counteracts the excessive sodium reabsorption and prevents fluid retention, over a prolonged period, chronically **elevated intraglomerular capillary pressures** contribute to glomerular structural changes. These include basement membrane thickening, mesangial expansion, and broadening of the podocyte foot processes, which result in the loss of small amounts of albumin in the urine (30-300 mg/day, or moderately increased albuminuria). **Albuminuria** is the earliest clinical sign of diabetic nephropathy and typically occurs before any appreciable rise in serum creatinine. Later in the disease process, there is widespread glomerulosclerosis and a decline in glomerular filtration.

(Choice A) The increased glomerular hydrostatic pressure seen in diabetic nephropathy results in excess water loss in the glomerulus during filtration. The water loss leads to increased concentration of the plasma proteins and increased (rather than decreased) peritubular oncotic pressure.

(Choice E) Increased oncotic pressure in Bowman's space occurs in diabetic nephropathy due to loss of albumin into the ultrafiltrate. However, this patient's urine assay shows no detectable albuminuria, so oncotic pressure would not be increased at this time.

Educational objective:
In diabetic nephropathy, early adaptive changes in the kidney cause a transient increase in glomerular filtration (hyperfiltration). As diabetic nephropathy progresses, glomerular filtration falls, with a concurrent increase in urine albumin loss.

References

- Renal hyperfiltration related to diabetes mellitus and obesity in human disease.

A 4-week-old, full-term boy is brought to the emergency department due to vomiting. His parents describe the emesis as undigested formula without blood or bile. The vomiting occurs after feeds and has increased in frequency and force over the past 6 days. He is afebrile. Blood pressure is normal, pulse is 182/min, and oxygen saturation of 98% on room air. Examination shows a thin, sleepy infant with a sunken anterior fontanelle and dry mucous membranes. Cardiac examination reveals tachycardia but no murmurs or gallops. The abdomen is soft, nontender, and nondistended. Arterial blood gas analysis is most likely to reveal which of the following sets of values?

	pH	$PaCO_2$	HCO_3^-	Anion gap
A.	7.29	30	14	Elevated
B.	7.30	55	26	Normal
C.	7.41	39	24	Normal
D.	7.49	46	34	Normal
E.	7.53	45	36	Elevated

Submit

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		pH	$PaCO_2$	HCO_3^-	Anion gap
	A. (6%)	7.29	30	14	Elevated
	B. (3%)	7.30	55	26	Normal
	C. (7%)	7.41	39	24	Normal
✓	D. (71%)	7.49	46	34	Normal
	E. (11%)	7.53	45	36	Elevated

Omitted
Correct answer
D

71%
Answered correctly

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Time Spent

04/15/2020
Last Updated

Explanation

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Omitted
Correct answer
D

71%
Answered correctly

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04/15/2020
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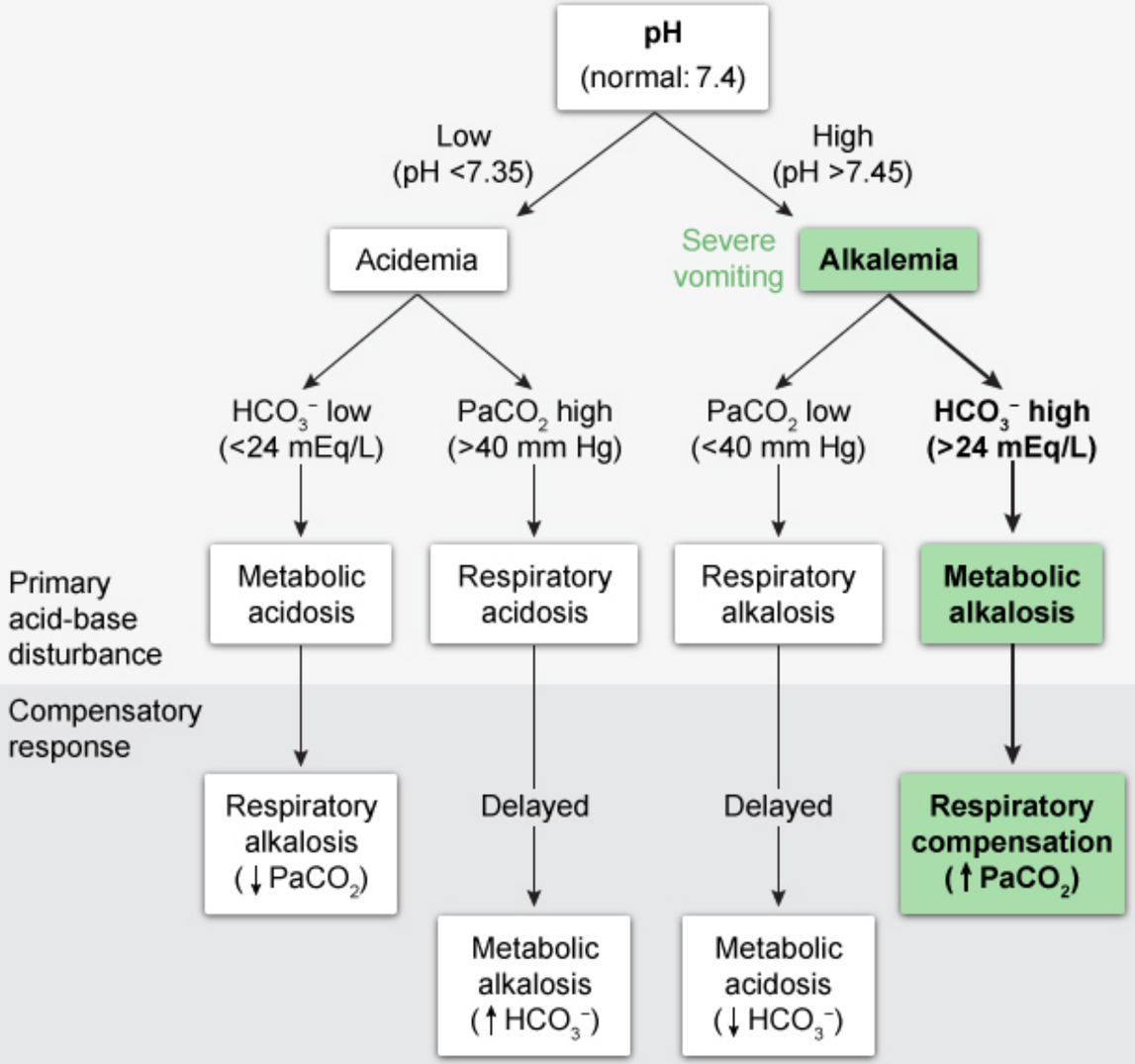
Explanation

Arterial blood gas interpretation of acid-base disorders



* The normal ranges for $PaCO_2$ and HCO_3^- vary slightly around 40 mm Hg and 24 mEq/L. For simplicity, these numbers should be used as a normal baseline for acid-base calculations.

HCO_3^- = bicarbonate; **$PaCO_2$** = partial pressure of carbon dioxide in arterial blood.

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This 4-week-old infant has had severe, nonbilious **vomiting** (suggesting pyloric stenosis) and now has multiple signs of **volume depletion** (eg, dry mucous membranes, sunken anterior fontanelle, tachycardia). **Primary metabolic alkalosis** (elevated pH >7.45, elevated HCO_3^- >24 mEq/L) with respiratory compensation ($PaCO_2$ >40 mm Hg) is the expected acid-base disturbance in such a setting.

With vomiting, there is loss of hydrochloric acid (H^+ and Cl^-) and fluid volume from the stomach. This causes metabolic alkalosis through multiple mechanisms:

- The **loss of H^+ ions** reduces the amount of carbonic acid (H_2CO_3) buffer in the body and increases the relative quantity of HCO_3^-.
- Volume loss and reduced oral intake lead to intravascular volume depletion and decreased renal perfusion, triggering activation of the renin-angiotensin-aldosterone system. Aldosterone stimulates Na^+ reabsorption in the distal tubules at the expense of **increased renal H^+ and K^+ excretion**.
- Hypovolemia, hypokalemia, and hypochloremia (from loss of hydrochloric acid) all contribute to impaired renal HCO_3^- excretion, leading to **increased renal HCO_3^- reabsorption**.
- Hypokalemia also causes cells to **exchange intracellular K^+ for extracellular H^+**, which increases serum potassium at the expense of decreased H^+ concentration (**increased blood alkalinity**).

Treatment of the underlying cause of vomiting and restoration of fluid volume with normal saline (typically with potassium repletion) is needed to resolve the hypokalemic, hypochloremic metabolic alkalosis.

(Choice A) Low pH and low HCO_3^- indicate metabolic acidosis, which can have a normal (eg, due to diarrhea or renal tubular acidosis) or elevated anion gap. $PaCO_2$ is low due to respiratory compensation.

(Choice B) Low pH and elevated $PaCO_2$ indicate respiratory acidosis. The near-normal HCO_3^- is consistent with minimal metabolic compensation, suggesting the respiratory acidosis is acute (eg, due to hypoventilation from opioid overdose).

- Hypovolemia, hypokalemia, and hypochloremia (from loss of hydrochloric acid) all contribute to impaired renal HCO_3^- excretion, leading to **increased renal HCO_3^- reabsorption**.
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(Choice B) Low pH and elevated $PaCO_2$ indicate respiratory acidosis. The near-normal HCO_3^- is consistent with minimal metabolic compensation, suggesting the respiratory acidosis is acute (eg, due to hypoventilation from opioid overdose).

(Choice C) These acid-base values are considered normal, indicating an absence of acid-base disturbance.

(Choice E) High pH and elevated HCO_3^- indicate metabolic alkalosis, with elevated $PaCO_2$ indicating respiratory compensation (as expected in this patient). However, because the anion gap is caused by unmeasured anions that donate H^+ and acidify the blood (eg, lactate/lactic acid), it is not significantly elevated in metabolic alkalosis.

Educational objective:
Severe vomiting leads to metabolic alkalosis through multiple mechanisms, including loss of H^+ from the gastrointestinal tract, volume and Cl^- depletion that induces renal retention of HCO_3^-, and hypokalemia-induced intracellular shifting of H^+. The anion gap is caused by unmeasured anions that acidify the blood; it is not significantly elevated in metabolic alkalosis.

References

- Physiology, metabolic alkalosis.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Metabolic alkalosis
Subject	System	Topic

Respiratory | Delayed | Delayed | Respiratory

This 4-week-old infant has
dry mucous membranes,
with respiratory compensa

With vomiting, there is los
mechanisms:

- The **loss of H^+ ions**
- Volume loss and re
angiotensin-aldoste
K^+ excretion.
- Hypovolemia, hypo
increased renal H
- Hypokalemia also c
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Treatment of the underlying cause of vomiting and restoration of fluid volume with normal saline (typically with potassium replenishment) is needed to

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Appropriate compensatory $PaCO_2$ or bicarbonate changes in acid-base disorders	
Metabolic acidosis (acute or chronic)	Expected $PaCO_2$ = (1.5 × bicarbonate) + 8 ± 2 (Winters formula)
Metabolic alkalosis (acute or chronic)	~7 mm Hg ↑ in $PaCO_2$ per 10 mEq/L ↑ in bicarbonate
Respiratory acidosis (chronic only*)	~4 mEq/L ↑ in bicarbonate per 10 mm Hg ↑ in $PaCO_2$
Respiratory alkalosis (chronic only*)	~4 mEq/L ↓ in bicarbonate per 10 mm Hg ↓ in $PaCO_2$

*Compensation for respiratory disturbances is minimal in the acute setting. The full level of chronic compensation is achieved after ~72 hr. For simplicity, normal baseline $PaCO_2$ and bicarbonate should be considered 40 mm Hg and 24 mEq/L, respectively.

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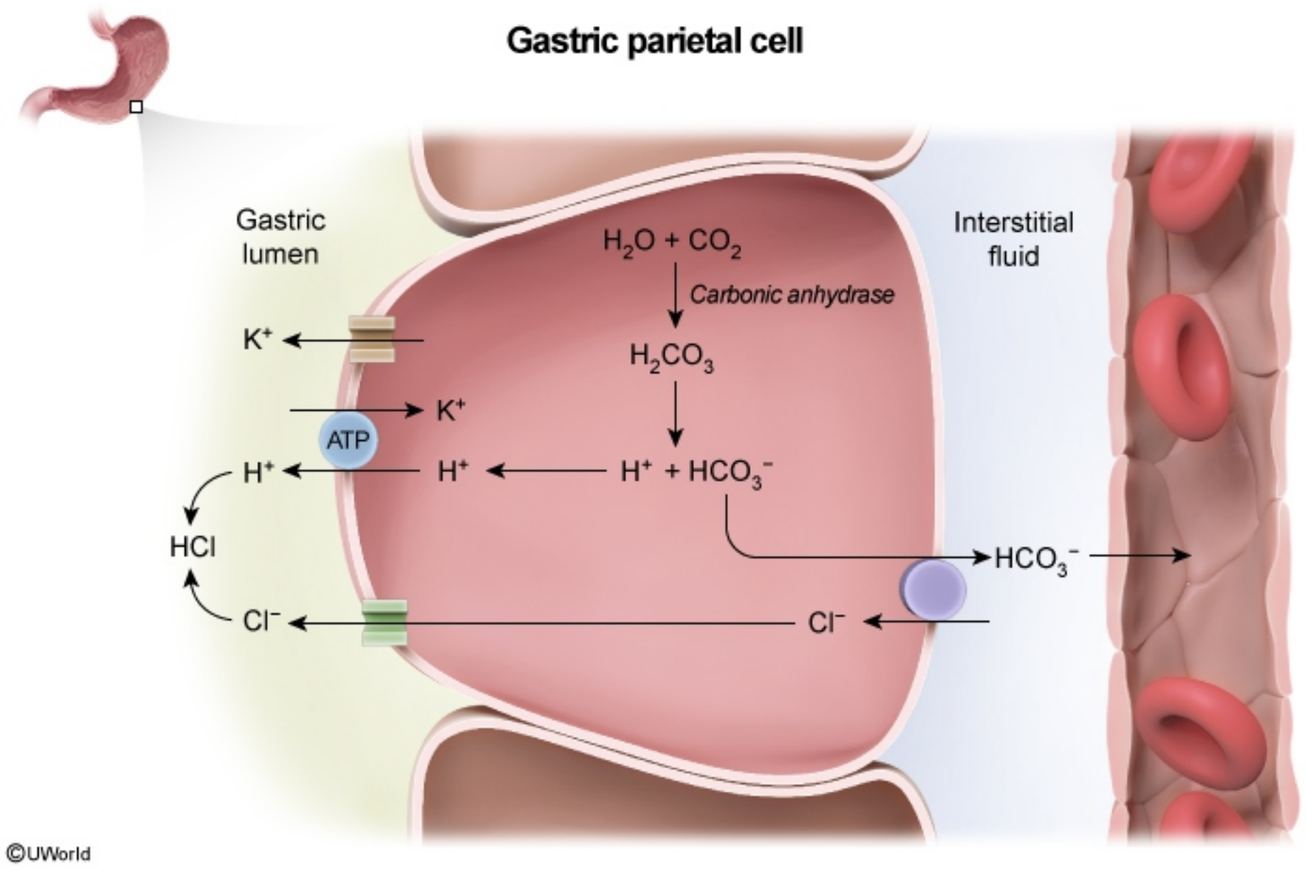

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Treatment of the underlying cause of vomiting and restoration of fluid volume with normal saline (typically with potassium repletion) is needed to

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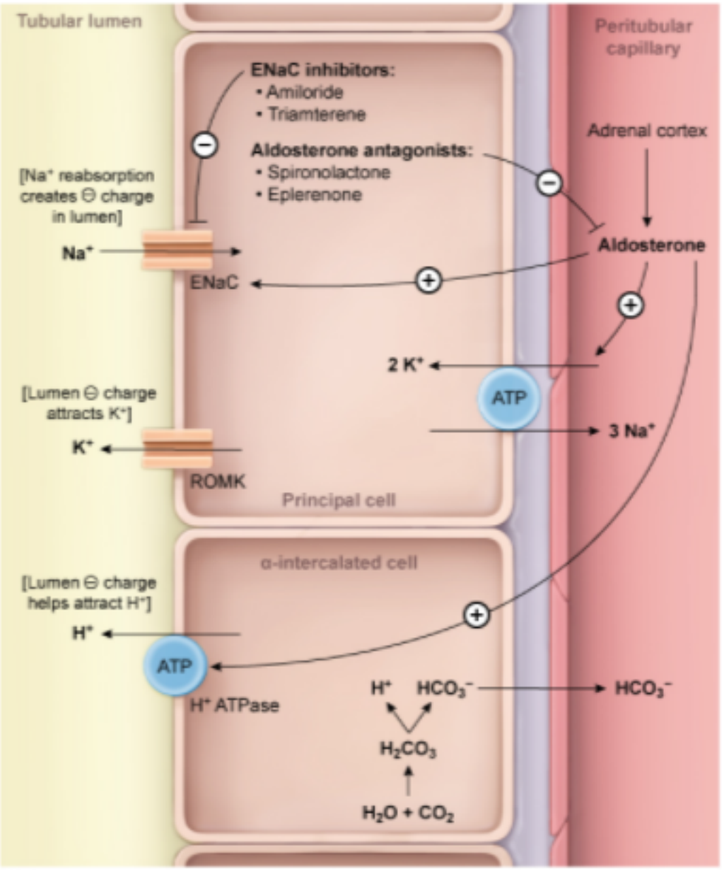
Action of aldosterone in the collecting duct of the nephron



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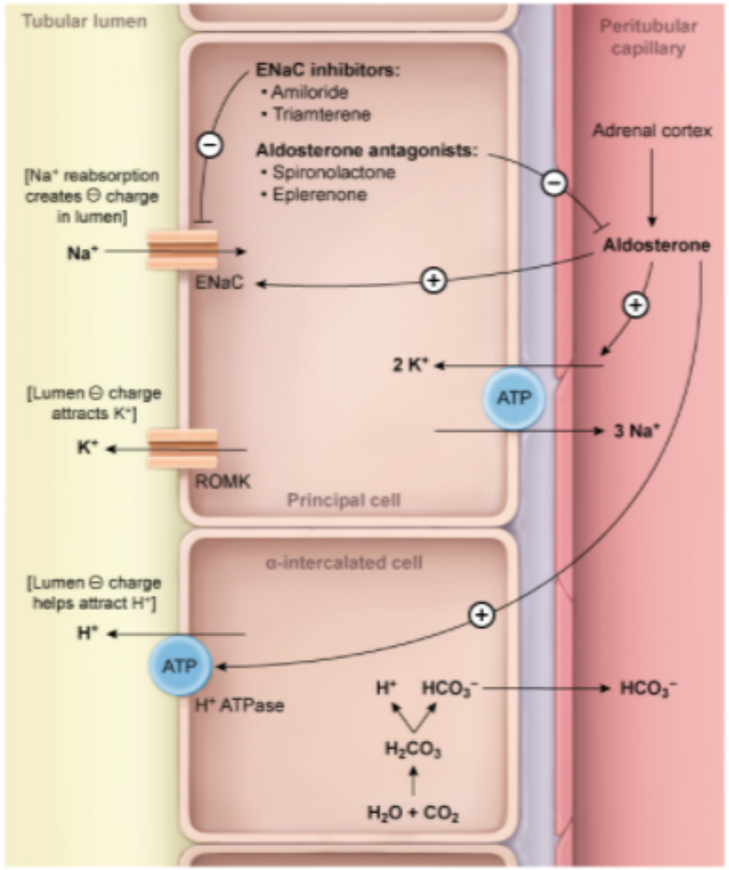
angiotensin-aldosterone system. Aldosterone stimulates Na^+ reabsorption in the distal tubules at the expense of **increased renal H^+ and**

Exhibit Display

Action of aldosterone in the collecting duct of the nephron



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- Hypovolemia, hypo
  increased renal H
- Hypokalemia also c
  decreased H^+ conce

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(Choice A) Low pH and l
elevated anion gap. PaC

(Choice B) Low pH and e
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(Choice C) These acid-b

(Choice E) High pH and
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not significantly elevated i

Educational objective:
Severe vomiting leads to
depletion that induces ren
anions that acidify the blo

References

- Physiology, metabolic

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Anion gap metabolic acidosis	
Calculation	Anion gap = sodium – (chloride + bicarbonate) (Normal: 10-14)
Common causes Mnemonic: MUDPILES	• Methanol • Uremia • Diabetic ketoacidosis • Propylene glycol/paraldehyde • Isoniazid/iron • Lactic acidosis • Ethylene glycol (antifreeze) • Salicylates (aspirin)

Add To Flash Card

An apparently healthy 6-year-old boy is enrolled in a research study designed to assess the amino acid absorptive capacity of the intestine. As part of the investigation, he is administered an oral solution containing free amino acids. Blood samples are then obtained at 15 minute intervals for the next 2 hours. The boy is found to have significantly decreased intestinal absorption of lysine, arginine, ornithine, and cysteine as compared to the other study participants. If his condition is left untreated, which of the following complications is this patient at greatest risk of developing?

A. Aortic dissection

B. Emphysema

C. Fat malabsorption

D. Intellectual disability

E. Kidney stones

F. Rickets

Submit

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- A. Aortic dissection (3%)
- B. Emphysema (0%)
- C. Fat malabsorption (4%)
- D. Intellectual disability (29%)
- ✓ E. Kidney stones (58%)
- F. Rickets (2%)

Omitted
Correct answer
E

58%
Answered correctly

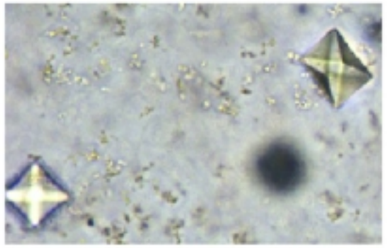
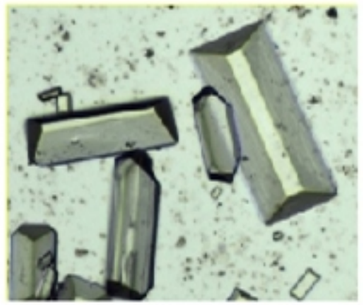
02 secs
Time Spent

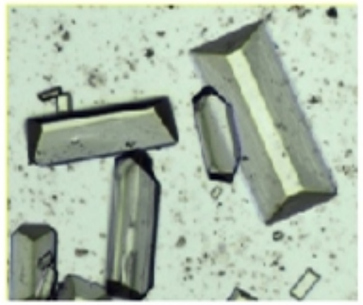
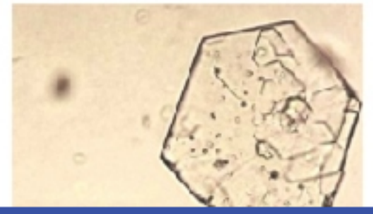
03/20/2020
Last Updated

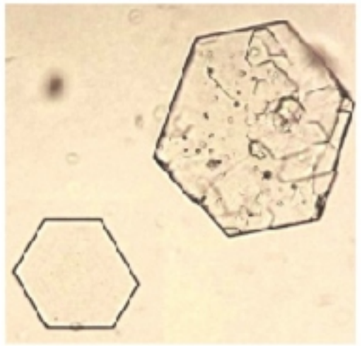
Explanation

Nephrolithiasis				
Content	Frequency	Radiograph	pH	Microscopic appearance

Nephrolithiasis

Content	Frequency	Radiograph opacity	pH	Microscopic appearance
Calcium oxalate	70%-80%	↑↑	--	 • Octahedron (square with an "X" in the center)
Calcium phosphate			>7.0	• Elongated, wedge-shaped • Forms rosettes
Magnesium ammonium phosphate (struvite or triple phosphate)	15%	↑	>7.0	 • Rectangular prism ("coffin lids")

Magnesium ammonium phosphate (struvite or triple phosphate)	15%	↑	>7.0	 • Rectangular prism ("coffin lids")
Uric acid	5%	--	<7.0	• Yellow or red-brown, diamond or rhombus
Cystine	1%	↑	<7.0	

Cystine	1%	↑	<7.0	 • Flat, yellow, **hexagonal**

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The dibasic amino acids **c**ysteine, **o**rnithine, **l**ysine, and **a**rginine (**cola**) share a common transporter in the intestinal lumen and kidneys. In patients with **cystinuria**, this transporter is defective, resulting in impaired renal and intestinal absorption of these amino acids.

- In the intestine, this causes absent (or diminished) intestinal absorption of these free amino acids. However, patients do not develop amino acid deficiencies, as these amino acids are absorbed in sufficient quantities as **oligopeptides**.
- In the kidneys, impaired tubular reabsorption of these amino acids leads to a high urinary cystine concentration, resulting in the formation of **cystine kidney stones**. The other amino acids (eg, ornithine, lysine, and arginine) are relatively soluble in urine and do not result in the formation of kidney stones.

Risk factors for cysteine precipitation include **low urine pH** (pH <7), the presence of a preexisting **crystal nidus**, and **urine supersaturation**.

(Choice A) Aortic dissection is a well-known complication of Marfan syndrome and other connective tissue disorders.

(Choice B) Emphysema is a common complication of α1-antitripsin deficiency. Liver involvement is also common in this disorder.

(Choice C) Fat malabsorption is typically seen in conditions that cause exocrine pancreas dysfunction, such as cystic fibrosis.

(Choice D) Intellectual disability occurs in several inborn errors of amino acid metabolism, including phenylketonuria, homocystinuria, and in

patients with **cystinuria**, this transporter is defective, resulting in impaired renal and intestinal absorption of these amino acids.

- In the intestine, this causes absent (or diminished) intestinal absorption of these free amino acids. However, patients do not develop amino acid deficiencies, as these amino acids are absorbed in sufficient quantities as **oligopeptides**.
- In the kidneys, impaired tubular reabsorption of these amino acids leads to a high urinary cystine concentration, resulting in the formation of **cystine kidney stones**. The other amino acids (eg, ornithine, lysine, and arginine) are relatively soluble in urine and do not result in the formation of kidney stones.

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(Choice B) Emphysema is a common complication of α1-antitripsin deficiency. Liver involvement is also common in this disorder.

(Choice C) Fat malabsorption is typically seen in conditions that cause exocrine pancreas dysfunction, such as cystic fibrosis.

(Choice D) Intellectual disability occurs in several inborn errors of amino acid metabolism, including phenylketonuria, homocystinuria, and in some patients with maple syrup urine disease (branched-chain ketoaciduria). However, intellectual disability is not seen in cystinuria.

(Choice F) Rickets is a failure of osteoid calcification (secondary to vitamin D deficiency) that occurs in children. This disorder is more likely to occur in infants who are exclusively breastfed, who receive no oral vitamin D supplementation, and who have darkly pigmented skin. Cystinuria does not affect bone calcification.

Educational objective:
Cystinuria is an autosomal recessive disorder caused by defective transportation of cystine, ornithine, arginine, and lysine across the intestinal and renal tubular epithelium. Recurrent nephrolithiasis is the only clinical manifestation. Urinalysis shows pathognomonic hexagonal cystine crystals.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Cystinuria
Subject	System	Topic

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A 45-year-old man comes to the emergency department due to urinary incontinence. He was diagnosed with multiple sclerosis a year ago after he developed transient acute vision loss in his right eye. A few weeks ago, he began having difficulty with his balance and had several episodes of urinary incontinence. The patient's walking has improved since, but he continues to urinate involuntarily. He has noticed increasing urinary frequency and cannot control the urge to urinate. His vital signs are normal. On examination, the patient has mild spastic paraparesis with increased reflexes in the lower extremities; bilateral Babinski sign; and a thoracic sensory level to pain, temperature, and vibration. An MRI of the spine reveals a new demyelinating lesion in the mid-thoracic spinal cord. Which of the following abnormalities will most likely be found on this patient's urodynamic studies?

A. Bladder hypertonia

B. Delayed bladder emptying

C. Elevated urethral pressure

D. Large residual volume of urine

E. Reduced urine flow

Submit

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- ✓ A. Bladder hypertonia (63%)
- B. Delayed bladder emptying (6%)
- C. Elevated urethral pressure (4%)
- D. Large residual volume of urine (23%)
- E. Reduced urine flow (2%)

Omitted
Correct answer
A

63%
Answered correctly

02 secs
Time Spent

06/07/2020
Last Updated

Explanation

This patient has urinary frequency and urge incontinence in the setting of an overactive or **spastic bladder** due to the presence of an **upper motor neuron lesion** in the spinal cord. Patients with **multiple sclerosis** often develop a spastic bladder a few weeks after developing an acute lesion of the spinal cord. **Urodynamic studies** show little or no residual urine after emptying as bladder contractility is normal but distensibility is

Explanation

This patient has urinary frequency and urge incontinence in the setting of an overactive or **spastic bladder** due to the presence of an **upper motor neuron lesion** in the spinal cord. Patients with **multiple sclerosis** often develop a spastic bladder a few weeks after developing an acute lesion of the spinal cord. **Urodynamic studies** show little or no residual urine after emptying as bladder contractility is normal but distensibility is poor. The **bladder does not distend/relax** properly due to loss of descending inhibitory control from the upper motor neuron.

(Choice B) This patient will have premature, as opposed to delayed, emptying due to his bladder overactivity. Delayed bladder emptying is more likely to occur in patients with diminished bladder tone.

(Choices C and E) Reduced urine flow and elevated urethral pressure indicate a mechanical obstruction (eg, enlarged prostate, urethral stricture) along the urinary tract.

(Choice D) Flaccid bladder typically occurs in the setting of lower motor neuron lesions (eg, cauda equina syndrome). A patient with a flaccid bladder will have a large residual volume of urine after attempted emptying and will typically experience urinary incontinence at the end of the day (pressure from a full bladder becomes greater than urinary sphincter pressure). In contrast, a patient with a spastic bladder will have frequent episodes of urinary incontinence throughout the day due to urgency.

Educational objective:
Patients with multiple sclerosis often develop a spastic bladder a few weeks after developing an acute lesion of the spinal cord. These patients present clinically with increased urinary frequency and urge incontinence. Urodynamic studies show the presence of bladder hypertonia.

References

- The neurogenic bladder in multiple sclerosis: review of the literature and proposal of management guidelines.
- The epidemiology and pathophysiology of neurogenic bladder.

Pathophysiology	Renal, Urinary Systems & Electrolytes	Urinary incontinence
Subject	System	Topic

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A 42-year-old man with a long history of type 1 diabetes mellitus comes to the office due to frequent involuntary loss of urine. For the past several months, he has been having difficulty starting and maintaining a urinary stream. In the last 3 weeks, he has had 2 episodes of nocturnal enuresis and multiple daytime episodes of uncontrolled voiding without any sensation of a full bladder. His other medical problems include chronic kidney disease and gastroparesis. He does not use tobacco or alcohol. Which of the following additional findings would most likely be present in this patient?

A. Enlarged prostate on rectal examination

B. Increased postvoid residual volume

C. Loss of sensation in perineal area

D. Lower extremity hyperreflexia

E. Mini-mental state examination score of 22

Submit

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- A. Enlarged prostate on rectal examination (12%)
- ✓ B. Increased postvoid residual volume (41%)
- C. Loss of sensation in perineal area (36%)
- D. Lower extremity hyperreflexia (8%)
- E. Mini-mental state examination score of 22 (0%)

Omitted
Correct answer
B

41%
Answered correctly

02 secs
Time Spent

04/05/2020
Last Updated

Explanation

This patient's findings suggest **overflow incontinence**, which is mainly due to **impaired detrusor contractility** or **bladder outlet obstruction** (eg, tumor obstructing the urethra). Patients usually develop involuntary and continuous urinary leakage when the bladder is full and often have incomplete emptying. This patient's overflow incontinence is most likely due to diabetic autonomic neuropathy affecting detrusor muscle innervation, which is common in type 1 diabetics.

Explanation

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Patients initially have infrequent urination due to loss of autonomic afferent innervation and inability to sense a full bladder. Involvement of efferent fibers to the bladder subsequently causes incomplete emptying. Patients can develop recurrent urinary tract infections (UTIs) and overflow incontinence with poor urinary stream and dribbling. Pelvic floor relaxation at night combined with a full bladder can lead to nocturnal enuresis. Postvoid residual (PVR) testing with ultrasound or catheterization can confirm inadequate bladder emptying.

(Choice A) Enlarged prostate on rectal examination may indicate either benign prostatic hyperplasia or prostate cancer, which causes urge incontinence (bladder irritation from the enlarged prostate) or overflow incontinence (urethral obstruction). However, these conditions are commonly seen in older individuals (age >50-60).

(Choice C) Loss of sensation in the perineal area (saddle anesthesia) can indicate cauda equina syndrome, which is commonly due to epidural cord compression from a malignancy. Patients usually develop urinary retention late in the course of the disease, usually associated with fecal incontinence.

(Choices D and E) Cognitive impairment (mini-mental status examination score ≤22) is often seen in normal pressure hydrocephalus, and lower extremity hyperreflexia would suggest spinal cord disease. Both of these conditions can cause loss of central nervous system inhibition of detrusor contraction, leading to urge incontinence. Urge incontinence is characterized by a sudden desire to urinate. However, absence of other symptoms (eg, gait disturbance) in this patient makes these conditions less likely.

Educational objective:
Diabetic autonomic neuropathy is common in type 1 diabetics and can cause overflow incontinence due to inability to sense a full bladder and incomplete emptying. Postvoid residual (PVR) testing with ultrasound or catheterization can confirm inadequate bladder emptying.

References

- Diagnosis of urinary incontinence.

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Pathophysiology	Renal, Urinary Systems & Electrolytes	Urinary incontinence
Subject	System	Topic

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